



# Title: Bioimpedance Devices for Detection and Management of Lymphedema

Professional / Institutional
Original Effective Date: September 12, 2023
Latest Review Date: March 12, 2024
Current Effective Date: September 12, 2023

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact <u>Blue Cross and Blue</u> <u>Shield of Kansas Customer Service</u>.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

Populations	Interventions	Comparators	Outcomes
<ul> <li>Individuals:</li> <li>With known or suspected lymphedema</li> </ul>	Interventions of interest are: • Bioimpedance spectroscopy	<ul> <li>Comparators of interest are:</li> <li>Volume displacement</li> <li>Circumferential measurement</li> </ul>	<ul> <li>Relevant outcomes</li> <li>include:</li> <li>Test validity</li> <li>Symptoms</li> <li>Quality of life</li> </ul>

# DESCRIPTION

Secondary lymphedema may develop following treatment for breast cancer. Bioimpedance, which uses resistance to electrical current to compare the composition of fluid compartments, could be used as a tool to diagnose lymphedema.

#### OBJECTIVE

The objective of this evidence review is to evaluate whether the use of bioimpedance spectroscopy devices improves the net health outcome for individuals with known or suspected lymphedema.

# BACKGROUND

#### Lymphedema

Lymphedema is an accumulation of fluid due to disruption of lymphatic drainage. Lymphedema can be caused by congenital or inherited abnormalities in the lymphatic system (primary lymphedema) but is most often caused by acquired damage to the lymphatic system (secondary lymphedema). Breast cancer treatment is one of the most common causes of secondary lymphedema. Both the surgical removal of lymph nodes and radiotherapy are associated with development lymphedema in individuals with breast cancer. In a systematic review of 72 studies (N=29,612 women), DiSipio et al (2013) reported that approximately 1 in 5 women who survive breast cancer will develop arm lymphedema.<sup>1,</sup> Risk factors for development of lymphedema that had a strong level of evidence were extensive surgery (ie, axillary-lymph-node dissection, greater number of lymph nodes dissected, mastectomy) and being overweight or obese.

#### **Diagnosis and Staging**

A diagnosis of secondary lymphedema is based on history (e.g., cancer treatment, trauma) and physical examination (localized, progressive edema and asymmetric limb measurements) when other causes of edema can be excluded. Imaging, such as MRI, computed tomography, ultrasound, or lymphoscintigraphy, may be used to differentiate lymphedema from other causes of edema in diagnostically challenging cases.

Table 1 lists International Society of Lymphology guidance for staging lymphedema based on "softness" or "firmness" of the limb and the changes with an elevation of the limb.<sup>2,</sup>

Stage	Description
Stage 0 (subclinical)	Swelling is not evident and most patients are asymptomatic despite impaired lymphatic transport
Stage I (mild)	Accumulation of fluid that subsides with limb elevation; soft edema that may pit, without evidence of dermal fibrosis
Stage II (moderate)	Does not typically resolve with limb elevation alone; limb may no longer pit on examination
Stage III (severe)	Lymphostatic elephantiasis; pitting can be absent; skin has trophic changes

Table 1. Recommendations for Staging Lymphedema

# **Management and Treatment**

Lymphedema is treated using elevation, compression, and exercise. Conservative therapy may consist of several features depending on the severity of the lymphedema. Individuals are educated on the importance of self-care including hygiene practices to prevent infection, maintaining ideal body weight through diet and exercise, and limb elevation. Compression therapy consists of repeatedly applying padding and bandages or compression garments. Manual

lymphatic drainage is a light pressure massage performed by trained physical therapists or by affected individuals designed to move fluid from obstructed areas into functioning lymph vessels and lymph nodes. Complete decongestive therapy is a multiphase treatment program involving all of the previously mentioned conservative treatment components at different intensities. Pneumatic compression pumps may also be considered as an adjunct to conservative therapy or as an alternative to self-manual lymphatic drainage in individuals who have difficulty performing self-manual lymphatic drainage. In individuals with more advanced lymphedema after fat deposition and tissue fibrosis has occurred, palliative surgery using reductive techniques such as liposuction may be performed.

#### **Bioimpedance Spectroscopy**

Bioimpedance spectroscopy is based on the theory that the level of opposition to the flow of electric current (impedance) through the body is inversely proportional to the volume of fluid in the tissue. In lymphedema, with the accumulation of excess interstitial fluid, tissue impedance decreases.

Bioimpedance has been proposed as a diagnostic test for this condition. In usual care, lymphedema is recognized clinically or via limb measurements. However, management via bioelectrical impedance spectroscopy has been proposed as a way to implement early treatment of subclinical lymphedema to potentially reduce its severity.

# **REGULATORY STATUS**

A selection of devices that have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process to aid in the assessment of lymphedema are summarized in Table 2.

Year	Device	Manufacturer	510(k) Number	Indication
2018	SOZO	ImpediMed (Carlsbad, CA)	K180126	For adults at risk of lymphedema. Supports the measurement of extracellular fluid volume differences between the limbs and is presented to the clinician on an L-Dex scale as an aid to their clinical assessment of lymphedema. The device is only indicated for patients who will have or who have had lymph nodes, from the axillary and/or pelvic regions, either removed, damaged, or irradiated.
2015	MoistureMeterD	Delfin Technologies (Stamford, CT)	K143310	Supports local assessment of tissue water differences between affected and contralateral non-affected arm tissues to aid in forming a clinical judgment of unilateral lymphedema in women. The device is not intended to make diagnosis or predict arm lymphedema.
2007	ImpediMed L- Dex™ U400	ImpediMed (Carlsbad, CA)	K050415	Supports the measurement of extracellular fluid volume differences between the arms to aid in the clinical assessment of unilateral lymphedema of the

#### Table 2. FDA Cleared Bioimpedance Spectroscopy Devices for Lymphedema

*Current Procedural Terminology* © American Medical Association. All Rights Reserved. Blue Cross and Blue Shield Kansas is an independent licensee of the Blue Cross Blue Shield Association

Year	Device	Manufacturer	510(k) Number	
				arm in women. This device is not intended to diagnose or predict lymphedema of an extremity.

FDA product code: OBH.

#### POLICY

Devices using bioimpedance (bioelectrical impedance spectroscopy) are considered **experimental / investigational** for use in the diagnosis, surveillance, or treatment of individuals with lymphedema, including use in subclinical secondary lymphedema.

# 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.

#### RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through November 27, 2023.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

# BIOIMPEDANCE SPECTROSCOPY IN INDIVIDUALS WITH KNOWN OR SUSPECTED LYMPHEDEMA

#### **Clinical Context and Test Purpose**

The purpose of using bioimpedance spectroscopy (BIS) in individuals who have known, or suspected lymphedema, is to inform a diagnosis of subclinical lymphedema to initiate treatment sooner than with other diagnostic methods.

The following PICO was used to select literature to inform this review.

#### **Populations**

The relevant population of interest is individuals with known or suspected lymphedema.

#### Interventions

The relevant intervention of interest is BIS.

Management via BIS has been proposed as a way to implement early treatment of subclinical lymphedema to potentially reduce its severity.

#### **Comparators**

The relevant comparators of interest are volume displacement and circumferential measurement.

In usual care, lymphedema is recognized clinically or via limb measurements.

Volume is measured using different methods; eg, tape measurements with geometry formulas, perometry, and water displacement.

#### Outcomes

Objective outcomes of interest include a reduction in limb circumference and/or volume and reduction in the rates of infections (eg, cellulitis, lymphangitis).

Patient-reported outcomes (PROs) of interest include symptoms, quality of life (QOL), and functional measures. A systematic review of PRO instruments and outcomes used to assess QOL in breast cancer patients with lymphedema, Pusic et al (2013) found that most studies included generic PRO instruments or oncology PRO instruments.<sup>3,</sup> Lymphedema-specific instruments are occasionally used; specifically, the Upper Limb Lymphedema 27 was found to have strong psychometric properties.

There does not appear to be a consensus on minimally clinically important change for either objective outcomes such as changes in arm volume or subjective measures such as changes to an individual's symptoms or QOL.

The time frame for outcomes varies from months to years after the onset of lymphedema symptoms.

#### **Study Selection Criteria**

For evaluation of clinical validity of bioimpedance testing, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores);
- Included a suitable reference standard;
- Patient/sample clinical characteristics were described;
- Patient/sample selection criteria were described.

For evaluation of clinical utility, comparative controlled prospective trials, with preference for RCTs were considered. In the absence of such trials, comparative observational studies, with preference for prospective studies were considered.

#### **Clinically Valid**

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

#### **Systematic Review**

A technology assessment on the diagnosis and treatment of secondary lymphedema, performed for the Agency for Healthcare Research and Quality (AHRQ), was published in 2010.<sup>4,</sup> The AHRQ assessment identified 8 studies that reported the sensitivity and specificity of tests to diagnose secondary lymphedema. Reviewers noted there is no true criterion standard to grade severity of lymphedema and that limb volume and circumference are used as de facto criterion standards. Two of the 8 selected studies evaluated BIS devices.<sup>5,6,</sup> Overall, reviewers concluded that, due largely to heterogeneity among studies, the evidence did not permit conclusions on the optimal diagnostic test for detection of secondary lymphedema.

A systematic review by Whitworth et al (2022) evaluated strategies for screening and early intervention in breast cancer patients at risk for lymphedema.<sup>7,</sup> A total of 12 studies (N=2907) were included. Although 4 RCTs were included, only 1 RCT evaluated BIS (see Ridner et al below). Of the 7 prospective, observational studies identified, 5 evaluated BIS. Although these studies generally point to BIS as a sensitive surveillance technique, this analysis did not synthesize data from the included studies and no quality or bias risk was assessed.

#### **Observational Studies**

After the AHRQ review, several other studies have evaluated the diagnostic performance of BIS devices for detecting lymphedema. Prospective studies that compared bioelectrical impedance analysis to a reference standard are described next.

A study by Barrio et al (2015) enrolled 223 women with newly diagnosed breast cancer and a plan for unilateral axillary surgery.<sup>8,</sup> Thirty-seven patients were excluded due to ineligibility or withdrawal, leaving a sample size of 186. Prior to surgery, participants received baseline volumetric measurements with a bioimpedance device (L-Dex) and volume displacement (the reference standard). Patients then had follow-up volumetric measurements every 3 to 6 months for 3 years. At the last follow-up (median, 18.2 months), 152 (82%) patients had no lymphedema, 21 (11%) had an abnormal L-Dex, and no lymphedema by volume displacement, 4 (2%) had an abnormal L-Dex and lymphedema by volume displacement, and 9 (5%) had lymphedema without prior L-Dex abnormality. In an analysis including only patients with at least 6 months of follow-up, L-Dex had a sensitivity of 31% (4/13) and a specificity of 88% (129/147) for predicting subsequent lymphedema development. Also, the correlation between changes in volume displacement and changes in L-Dex results were in the low-to-moderate range at 3 months (*r*=0.31) and 6 months (*r*=0.21). However, at the time of lymphedema diagnosis, the L-Dex ratio was abnormal in 12 of 13 patients (diagnostic sensitivity, 92%).

Blaney et al (2015) reported on a prospective study with 126 women with stage I, II, or III unilateral breast cancer.<sup>9,</sup> A total of 115 women underwent baseline assessment with an L-Dex and circumferential measurement. The circumferential measurement was used as the reference standard, although the authors noted the test is an imperfect criterion standard. Postsurgical follow-up assessments were planned every 3 months for a year. The number of women completing these assessments was 109 (95%) at 3 months, 89 (77%) at 6 months, 79 (69%) at 9 months, and 71 (62%) at 12 months. Over 12 months, 31 participants were identified as having lymphedema by at least 1 of the assessment methods. Twenty-eight (90%) of 31 were identified by circumferential measurement and 11 (35%) by BIS. There was no statistically significant correlation between bioimpedance analysis and circumferential measurement.

# **Clinically Useful**

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if individuals receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

The ideal study design is an RCT comparing health outcomes in individuals managed with and without the use of bioimpedance devices.

# **Randomized Controlled Trial**

One multicenter, international, RCT conducted by Ridner et al (2019 and 2022) compared bioimpedance to volume measurements calculated from arm circumference using a tape measure (Table 3).<sup>10,11,</sup> The primary aim of the study was to determine if subclinical detection of extracellular fluid accumulation via BIS and subsequent early intervention reduces the rate of progression to clinical lymphedema relative to the rates seen using standard tape measurements. Patients requiring early intervention were prescribed a compression sleeve and gauntlet for 4 weeks and then re-evaluated. Predetermined thresholds were used to trigger early intervention. The implementation threshold for patients in the bioimpedance group was initially a change that was  $\geq$ 10 L-Dex units (3 standard deviations) higher than the presurgical baseline measure, but the protocol was changed in 2016 to include all patients with  $\geq$ 6 L-Dex units. Patients in the tape measure group triggered when they had a volume change in the at-risk arm that was between >5 and <10% above the presurgical baselines. Progression to clinical lymphedema was defined as a 10% or greater increase in tape measure volume from baseline in the at-risk arm.

Results of the interim analysis and final analysis are summarized in Table 4.<sup>11,10,</sup> At interim analysis , 109 of 508 (21.9%) patients received early intervention due to reaching the predetermined threshold. Patients randomized to bioimpedance had a lower rate of trigger and longer times to trigger. A total of 12 triggering patients progressed to clinical lymphedema (10 in the TM group [14.7%] and 2 in the BIS group [4.9%]). The difference between groups was not statistically significant (p=.130) and did not meet stopping criteria specified in the study protocol. At final analysis (median of 32.9 months follow-up), BIS triggered an intervention at a lower rate than TM patients (20.1% vs 27.5%; p=.011); however, fewer patients in the BIS group progressed compared with tape measure (7.9% vs 19.2%; relative risk, 0.41; 95% CI, 2.8-4.5; p=.001).

This study had several limitations (see Tables 5 and 6), including an open-label design, which may have introduced bias in outcome assessment, treatments, or the decision to trigger an intervention. Important health outcomes such as patient-reported symptoms, QOL, and function were not assessed. Additionally, 39 patients who progressed prior to an intervention being triggered were excluded from the analysis.

Study; Trial	Country	Sites	Dates	Participants	Intervention	ons
					Active	Comparator
Ridner et al (2019 and 2022) <sup>11,10,</sup> PREVENT- NCT02167659	U.S. and Australia	13	2014-2018	Presurgical: Women >18 years of age with histologically confirmed, newly diagnosed, breast cancer (invasive or DCIS) with planned surgery. Postsurgical: stage I–III invasive breast cancer or DCIS who received ≥1 of the following: mastectomy, axillary treatment, regional node irradiation, or taxane-based chemotherapy	BIS: N=263 at interim; 482 at final	Tape measure: N=245 at interim; 481 at final

Table 3. Summary of Key RCT Characteristics

BIS: bioimpedance spectroscopy; DCIS: ductal carcinoma in situ; NCT: national clinical trial; PREVENT: Bioimpedance Spectroscopy Versus Tape Measure in Prevention of Lymphedema; RCT: randomized controlled trial.

# Table 4. Summary of Key RCT Results

Study	Intervention triggered	Median (IQR) months to intervention triggered	Progression to clinical lymphedema	Median (range) months to progression to clinical lymphedema
Ridner et al (2019) <sup>11,</sup>				
BIS	41/259 (15.8%)	2.8 (0.6–5.6)	2/41 (4.9%)	6.0 (1.4, 16.9)
Tape measure	68/239 (28.5%)	4.0 (1.0–11.2)	10/68 (14.7%)	6.0 (0.8, 16.9))
p-value	.001	.002	.130	.389

*Current Procedural Terminology* © American Medical Association. All Rights Reserved. Blue Cross and Blue Shield Kansas is an independent licensee of the Blue Cross Blue Shield Association

Study	Intervention triggered	Median (IQR) months to intervention triggered	Progression to clinical lymphedema	Median (range) months to progression to clinical lymphedema
Ridner et al (2022) <sup>10,</sup>				
BIS	89/442 (20.1%)	9.7 (3.6-18.2)	7/89 (7.9%)	4.9 (0.7-15.2)
Tape measure	120/437 (27.5%)	3.9 (1.0-11.6)	23/120 (19.2%)	10.7 (1.4-31.9)
p-value	.011	.001	.016	.100

BIS: bioimpedance spectroscopy; IQR: interquartile range; RCT: randomized controlled trial;.

#### Table 5. Study Relevance Limitations

Study	Population <sup>a</sup>	Intervention <sup>b</sup>	Comparator <sup>c</sup>	Outcomes <sup>d</sup>	Duration of Follow-Up <sup>e</sup>
Ridner et al (2019 and 2022) <sup>11,10,</sup>				1. Patient- reported outcomes not assessed	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

<sup>b</sup> Intervention key: 1. Classification thresholds not defined; 2. Version used unclear; 3. Not intervention of interest. <sup>c</sup> Comparator key: 1. Classification thresholds not defined; 2. Not compared to credible reference standard; 3. Not compared to other tests in use for same purpose.

<sup>d</sup> Outcomes key: 1. Study does not directly assess a key health outcome; 2. Evidence chain or decision model not explicated; 3. Key clinical validity outcomes not reported (sensitivity, specificity, and predictive values); 4. Reclassification of diagnostic or risk categories not reported; 5. Adverse events of the test not described (excluding

minor discomforts and inconvenience of venipuncture or noninvasive tests). <sup>e</sup> Follow-Up key: 1. Follow-up duration not sufficient with respect to natural history of disease (true-positives, truenegatives, false-positives, false-negatives cannot be determined).

Study	Selection <sup>a</sup>	Blinding <sup>b</sup>	Delivery of Test <sup>c</sup>	Selective Reporting <sup>d</sup>	Data Completeness <sup>e</sup>	Statistical <sup>f</sup>
Ridner et al (2019 and 2022) <sup>11,10,</sup>		1. Open- label			2. 10 patients who progressed prior to triggered intervention were excluded from interim and 39 from final analysis	

 Table 6. Study Design and Conduct Limitations

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

<sup>a</sup> Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).

<sup>b</sup> Blinding key: 1. Not blinded to results of reference or other comparator tests.

<sup>c</sup> Test Delivery key: 1. Timing of delivery of index or reference test not described; 2. Timing of index and comparator tests not same; 3. Procedure for interpreting tests not described; 4. Expertise of evaluators not described.
 <sup>d</sup> Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
 <sup>e</sup> Data Completeness key: 1. Inadequate description of indeterminate and missing samples; 2. High number of samples excluded; 3. High loss to follow-up or missing data.

<sup>f</sup> Statistical key: 1. Confidence intervals and/or p values not reported; 2. Comparison with other tests not reported.

#### **Observational Studies**

One prospective observational study compared clinical lymphedema rates in patients managed with and without bioimpedance analysis. This study, by Soran et al (2014), involved prospective detection of subclinical lymphedema in 186 women with breast cancer managed with L-Dex or tape measurement of limb circumference.<sup>12,</sup> Measurements were obtained at baseline and 3- to 6-month intervals for 5 years. Subclinical lymphedema was defined as an L-Dex value outside the normal range, or that increased at least 10 units from baseline. Patients diagnosed with subclinical lymphedema were treated with, eg, short-term physical therapy, compression garments, and received education on exercise and limb elevation. A total of 180 women were included in the analysis. Seventy-two women had both preoperative and postoperative bioimpedance and tape measurements (preoperative group). Forty-four women had preoperative bioimpedance and tape measurements but only had tape measurements postoperatively (control group). The remaining 64 women had postoperative bioimpedance and tape measurements (no preoperative group). The authors compared the demographic and clinical characteristics of the preoperative and control groups and the preoperative and postoperative and control groups and the preoperative and postoperative and postoperative and postoperative and postoperative and postoperative and control groups and the preoperative and postoperative and postope

In the preoperative group, 28 (36%) of 72 women were diagnosed with subclinical lymphedema and referred for treatment; 2 women progressed to clinical lymphedema. In the control group, 16 women (36%) developed clinical lymphedema during follow-up. Limitations of the study included a lack of an alternative method for detecting subclinical lymphedema in women in the control group so that they could receive treatment early; a lack of randomization to a treatment group; and incomplete data on pre- and postoperative measures of lymphedema except in a subset of the total population.

Multiple uncontrolled observational studies have reported rates of lymphedema identified through surveillance with bioimpedance in women at high-risk following breast cancer treatment.<sup>13,14,15,16,17,18,19,20,21,22</sup>, Because these studies did not include a comparison group of women who received usual care or alternative methods of screening, they do not provide evidence to draw conclusions about the clinical utility of bioimpedance.

# Section Summary: Bioimpedance Spectroscopy in Individuals With Known or Suspected Lymphedema

A 2010 AHRQ technology assessment identified few studies on BIS analysis for diagnosing lymphedema. A 2022 systematic review identified the PREVENT trial as the primary evidence evaluating BIS for lympedema surveillance. Results from the PREVENT RCT comparing BIS with standard tape measure following treatment for breast cancer have been published. At a median follow-up of 32.9 months, BIS patients triggered intervention at a lower rate than tape measure patients (20.1% vs 27.5%) and fewer patients progressed in this group (7.9% vs 19.2%). Additional studies to confirm these findings are needed, especially RCTs and trials that include an alternative method for early or subclinical lymphedema detection.

#### SUPPLEMENTAL INFORMATION

The purpose of the remaining sections in Supplemental Information is to provide reference material regarding existing practice guidelines and position statements, U.S. Preventive Services Task Force Recommendations and Medicare National Coverage Decisions and registered, ongoing clinical trials. Inclusion in the Supplemental Information does not imply endorsement and information may not necessarily be used in formulating the evidence review conclusions.

### **Clinical Input From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 2 specialty societies and 2 academic medical centers while this policy was under review in 2011. Three of 4 reviewers agreed that bioimpedance devices are considered investigational for diagnosis, surveillance, and treatment of patients with lymphedema. The fourth reviewer, from an academic medical center, considered the use of the technology a reasonable alternative, especially in situations in which minor lymphedema can have a large impact on a patient. One specialty society supported further research into the effectiveness of this technology and recommended reimbursement in the context of relevant clinical trials.

#### **Practice Guidelines and Position Statements**

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

#### National Comprehensive Cancer Network

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines on Survivorship (v.1.2023) recommends that survivors at risk for lymphedema should be regularly screened for lymphedema by symptom assessment, clinical exam, and, if available, bioimpedance spectroscopy.<sup>23,</sup>

NCCN Clinical Practice Guidelines on Breast Cancer (v.4.2023) recommend education, monitoring, and referral for lymphedema management as needed. For further information they refer the reader to the Survivorship Guidelines.<sup>24,</sup>

# **U.S. Preventive Services Task Force Recommendations**

Not applicable.

#### **Ongoing and Unpublished Clinical Trials**

Some currently ongoing and unpublished trials that might influence this review are listed in Table 7.

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03978754	Assessment of Breast Cancer-Related Arm Lymphedema— Comparison of Traditional Measurement Methods and Indocyanine Green (ICG) Lymphography	1600	Jan 2022 (status unknown )
NCT02743858	A Prospective Surveillance Program for Assessment and Treatment of Breast Cancer-Related Lymphedema After Axillary Lymph Node Dissection	850	Apr 2024 (Recruiting as of Nov 2023 )
Unpublished			
NCT01544335	Evaluation of the Validity of BIS as a Tool for Quantification of Lymphedema Through Comparison With Perometry and Self-Report	270	Sept 2020

**Table 7. Summary of Key Trials** 

BIS: bioimpedance spectroscopy; NCT: national clinical trial.

#### CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. 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.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

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

REVISIONS	
09-12-2023	Policy added to the bcbsks.com web site.
03-12-2024	Update Description Section
	Updated Rationale Section
	Updated References Section

#### REFERENCES

- 1. DiSipio T, Rye S, Newman B, et al. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. Lancet Oncol. May 2013; 14(6): 500-15. PMID 23540561
- International Society of Lymphology Executive Committee. The Diagnosis and Treatment of Peripheral Lymphedema: 2020 Consensus Document of the International Society of Lymphology. 2020; https://isl.arizona.edu/sites/default/files/2021-09/Consensus%20Document-SM.pdf. Accessed November 27, 2023.
- 3. Pusic AL, Cemal Y, Albornoz C, et al. Quality of life among breast cancer patients with lymphedema: a systematic review of patient-reported outcome instruments and outcomes. J Cancer Surviv. Mar 2013; 7(1): 83-92. PMID 23212603
- 4. Oremus M, Walker K, Dayes I, et al. Technology Assessment: Diagnosis and treatment of secondary lymphedema. Rockville, MD: Agency for Healthcare Research and Quality; 2010.
- 5. Cornish BH, Chapman M, Hirst C, et al. Early diagnosis of lymphedema using multiple frequency bioimpedance. Lymphology. Mar 2001; 34(1): 2-11. PMID 11307661
- 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. Mar 2008; 41(1): 18-28. PMID 18581955
- 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. J Cancer Surviv. Aug 10 2022. PMID 35947288

- 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. Dec 2015; 22 Suppl 3(0 3): S370-5. PMID 26085222
- 9. Blaney JM, McCollum G, Lorimer J, et al. Prospective surveillance of breast cancer-related lymphoedema in the first-year post-surgery: feasibility and comparison of screening measures. Support Care Cancer. Jun 2015; 23(6): 1549-59. PMID 25398360
- 10. 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. Dec 2022; 20(6): 618-628. PMID 35099283
- 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. Oct 2019; 26(10): 3250-3259. PMID 31054038
- Soran A, Ozmen T, McGuire KP, et al. The importance of detection of subclinical lymphedema for the prevention of breast cancer-related clinical lymphedema after axillary lymph node dissection; a prospective observational study. Lymphat Res Biol. Dec 2014; 12(4): 289-94. PMID 25495384
- Laidley A, Anglin B. The Impact of L-Dex(®) Measurements in Assessing Breast Cancer-Related Lymphedema as Part of Routine Clinical Practice. Front Oncol. 2016; 6: 192. PMID 27656420
- 14. Koelmeyer LA, Borotkanics RJ, Alcorso J, et al. Early surveillance is associated with less incidence and severity of breast cancer-related lymphedema compared with a traditional referral model of care. Cancer. Mar 15 2019; 125(6): 854-862. PMID 30521080
- Kilgore LJ, Korentager SS, Hangge AN, et al. Reducing Breast Cancer-Related Lymphedema (BCRL) Through Prospective Surveillance Monitoring Using Bioimpedance Spectroscopy (BIS) and Patient Directed Self-Interventions. Ann Surg Oncol. Oct 2018; 25(10): 2948-2952. PMID 29987599
- Whitworth PW, Cooper A. Reducing chronic breast cancer-related lymphedema utilizing a program of prospective surveillance with bioimpedance spectroscopy. Breast J. Jan 2018; 24(1): 62-65. PMID 29063664
- 17. 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. Mar 2015; 13(1): 40-5. PMID 25526543
- Shah C, Vicini F, Beitsch P, et al. The use of bioimpedance spectroscopy to monitor therapeutic intervention in patients treated for breast cancer related lymphedema. Lymphology. Dec 2013; 46(4): 184-92. PMID 25141461
- 19. Lim SM, Han Y, Kim SI, et al. Utilization of bioelectrical impedance analysis for detection of lymphedema in breast Cancer survivors: a prospective cross sectional study. BMC Cancer. Jul 08 2019; 19(1): 669. PMID 31286884
- 20. Kaufman DI, Shah C, Vicini FA, et al. Utilization of bioimpedance spectroscopy in the prevention of chronic breast cancer-related lymphedema. Breast Cancer Res Treat. Dec 2017; 166(3): 809-815. PMID 28831632
- Whitworth PW, Shah C, Vicini F, et al. Preventing Breast Cancer-Related Lymphedema in High-Risk Patients: The Impact of a Structured Surveillance Protocol Using Bioimpedance Spectroscopy. Front Oncol. 2018; 8: 197. PMID 29946531
- 22. Jeffers EJ, Wagner JL, Korentager SS, et al. Breast Cancer-Related Lymphedema (BCRL) and Bioimpedance Spectroscopy: Long-Term Follow-Up, Surveillance Recommendations,

and Multidisciplinary Risk Factors. Ann Surg Oncol. Oct 2023; 30(10): 6258-6265. PMID 37535267

- National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Survivorship. Version 1.2023. Updated March 24, 2023. https://www.nccn.org/professionals/physician\_gls/pdf/survivorship.pdf. Accessed November 27, 2023.
- National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Breast Cancer. Version 4.2023. Updated March 23, 2023. https://www.nccn.org/professionals/physician\_gls/pdf/breast.pdf. Accessed November 26, 2023.