Bioimpedance Devices for Detection and Management of Lymphedema

Policy Number: 2.01.82
Origination: 1/2011
Last Review: 5/2020
Next Review: 5/2021

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for bioimpedance devices for detection of lymphedema. This is considered investigational.

When Policy Topic is covered
Not Applicable

When Policy Topic is not covered
Devices using bioimpedance (bioelectrical impedance spectroscopy) are considered investigational for use in the diagnosis, surveillance, or treatment of patients with lymphedema, including use in subclinical secondary lymphedema.

Bioimpedance, which uses resistance to electrical current in comparing the composition of fluid compartments, could potentially be used as a tool to diagnose lymphedema. There is minimal information about the technical and diagnostic performance of bioimpedance testing in the diagnosis (surveillance) of secondary lymphedema; especially for subclinical disease. In addition, there are no data from comparative clinical trials that demonstrate the impact of this test (bioimpedance) on clinical outcomes (clinical utility). Thus, based on the current scientific evidence and because the impact on net health outcome is not known, use of this testing in the diagnosis or management of patients with known or suspected lymphedema, or to detect subclinical lymphedema, is considered investigational.

Description of Procedure or Service

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td></td>
<td>▪ With known or suspected lymphedema</td>
<td>▪ Bioimpedance spectroscopy</td>
<td>▪ Test validity</td>
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<tr>
<td></td>
<td></td>
<td>▪ Volume displacement</td>
<td>▪ Symptoms</td>
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<td></td>
<td></td>
<td>▪ Circumferential measurement</td>
<td>▪ Quality of life</td>
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</tbody>
</table>
Secondary lymphedema may develop following surgery for breast cancer. Bioimpedance, which uses resistance to electrical current in comparing the composition of fluid compartments, could potentially be used as a tool to diagnose lymphedema.

For individuals who have known or suspected lymphedema who receive bioimpedance spectroscopy, the evidence includes a systematic review, one RCT, one prospective comparative observational study, and multiple uncontrolled observational studies. The relevant outcomes are test validity, symptoms, and quality of life. Diagnostic accuracy studies have found a poor correlation between bioimpedance analysis and the reference standard (volume displacement or circumferential measurement). Interim results from an ongoing RCT comparing bioimpedance with standard tape measure following treatment for breast cancer have been published. Overall, 109 of 508 (21.5%) patients received early treatment due to reaching a pre-determined threshold to trigger an intervention. A total of 12 triggering patients progressed to clinical lymphedema (2 in the bioimpedance group [4.9%] and 10 in the tape measure group [14.7%]; P=0.130). The RCT was limited by its open-label design and lack of reporting of important health outcomes. The single prospective comparative study found a significantly lower rate of clinical lymphedema in patients managed with bioimpedance devices but had several limitations, including nonrandomized design, lack of blinding, lack of complete data on a substantial proportion of enrolled patients, and lack of a systematic method for diagnosing lymphedema in the control group. Retrospective studies suggested that postoperative bioimpedance monitoring is feasible but provide limited information about its efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

**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 patients with breast cancer. In a systematic review of 72 studies (N=29612 women), DiSipio et al (2013) reported that approximately 1 in 5 women who survive breast cancer will develop arm lymphedema. 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.2

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0 (subclinical)</td>
<td>Swelling is not evident and most patients are asymptomatic despite impaired lymphatic transport</td>
</tr>
<tr>
<td>Stage I (mild)</td>
<td>Accumulation of fluid that subsides (usually within 24 hours) with limb elevation; soft edema that may pit, without evidence of dermal fibrosis</td>
</tr>
<tr>
<td>Stage II (moderate)</td>
<td>Does not resolve with limb elevation alone; limb may no longer pit on examination</td>
</tr>
<tr>
<td>Stage III (severe)</td>
<td>Lymphostatic elephantiasis; pitting can be absent; skin has trophic changes</td>
</tr>
</tbody>
</table>

**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. Patients 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 patients 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 patients who have difficulty performing self-manual lymphatic drainage. In patients 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**

Devices that have been cleared for marketing by the FDA through the 510(k) process to aid in the assessment of lymphedema are summarized in Table 2.

**Table 2. FDA-Cleared Bioimpedance Spectroscopy Devices for Lymphedema**

<table>
<thead>
<tr>
<th>Year</th>
<th>Device</th>
<th>Manufacturer</th>
<th>510(k) Number</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>SOZO</td>
<td>ImpediMed (Carlsbad, CA)</td>
<td>K180126</td>
<td>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.</td>
</tr>
<tr>
<td>2015</td>
<td>MoistureMeterD</td>
<td>Delfin Technologies (Stamford, CT)</td>
<td>K143310</td>
<td>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.</td>
</tr>
<tr>
<td>2007</td>
<td>ImpediMed L-Dex™ U400</td>
<td>ImpediMed (Carlsbad, CA)</td>
<td>K050415</td>
<td>Supports the measurement of extracellular fluid volume differences between the arms to aid in the clinical assessment of unilateral lymphedema of the arm in women. This device is not intended to diagnose or predict lymphedema of an extremity.</td>
</tr>
</tbody>
</table>

FDA product code: OBH.

**Rationale**

This evidence review was created in March 2010 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through November 14, 2019.

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.

**Bioimpedance Spectroscopy in Patients With Known or Suspected Lymphedema**

**Clinical Context and Test Purpose**
The purpose of using BIS in patients who have known, or suspected lymphedema, is to inform a diagnosis of subclinical lymphedema to initiate treatment sooner than with other diagnostic methods.

The question addressed in this evidence review is: Does the use of BIS devices detect lymphedema in individuals with known or suspected lymphedema?

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

**Population**
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.

The intervention would be used during a physical exam conducted by a physician in an inpatient or outpatient setting.

**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.3 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 patient 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.

**Technical Reliability**

Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on clinical validity and clinical utility.

**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 2010.4 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 eight selected studies evaluated bioimpedance...
devices. 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.

**Observational Studies**

After the AHRQ review, several other studies have evaluated the diagnostic performance of bioimpedance 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. 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. 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.

**Section Summary: Clinically Valid**

A 2010 AHRQ technology assessment identified few studies on bioimpedance analysis for diagnosing lymphedema. A few prospective studies, published after the AHRQ review, found suboptimal correlations between bioimpedance analysis and the reference standard. In the study that reported measures of diagnostic accuracy, bioimpedance analysis had low sensitivity and specificity for predicting lymphedema development.
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 patients 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 patients managed with and without the use of bioimpedance devices.

Randomized Controlled Trial
One RCT compared bioimpedance to volume measurements calculated from arm circumference using a tape measure (Table 3). The study is ongoing but preliminary results on the first 508 patients have been published. The interim analysis was preplanned to be performed when at least 500 participants reached at least 12 months of follow-up. The primary aim of the study was to determine if subclinical detection of extracellular fluid accumulation via bioimpedance 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 a change that was >10 L-Dex units (3 standard deviations) higher than the presurgical baseline measure. 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 are summarized in Table 4. Overall, 109 of 508 (21.9%) patients received early intervention due to reaching the pre-determined 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=0.130) and did not meet stopping criteria specified in the study protocol. The study is expected to be completed in December 2020 with a total of 1100 patients.

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, 10 patients who progressed prior to an intervention being triggered were excluded from the analysis.
Table 3. Summary of Key RCT Characteristics

<table>
<thead>
<tr>
<th>Study; Trial</th>
<th>Country</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ridner et al (2019)*</td>
<td>U.S.</td>
<td>10</td>
<td>2014-2018</td>
<td>Pressurgical: Women &gt;18 years of age with histologically confirmed breast cancer (invasive or ductal carcinoma in situ with planned surgery Postsurgical: stage I–III invasive breast cancer or DCIS who received mastectomy, axillary treatment, and/or taxane-based chemotherapy</td>
<td>Bioimpedance N=263</td>
</tr>
</tbody>
</table>

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

Table 4. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Triggered</th>
<th>Median (IQR) months to Intervention Triggered</th>
<th>Progression to clinical lymphedema</th>
<th>Median (range) months to progression to clinical lymphedema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ridner et al (2019)*</td>
<td>41/259 (15.8%)</td>
<td>2.8 (0.6–5.6)</td>
<td>2/41 (4.9%)</td>
<td>6.0 (1.4, 16.9)</td>
</tr>
<tr>
<td>Bioimpedance</td>
<td>68/239 (28.5%)</td>
<td>4.0 (1.0–11.2)</td>
<td>10/68 (14.7%)</td>
<td>6.0 (0.8, 16.9))</td>
</tr>
<tr>
<td>Tape measure</td>
<td>0.001</td>
<td>0.002</td>
<td>0.130</td>
<td>0.389</td>
</tr>
</tbody>
</table>

P-value 0.001 0.002 0.130 0.389

RCT: randomized controlled trial; IQR: interquartile range.

Table 5. Relevance Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Populationa</th>
<th>Interventionb</th>
<th>Comparatorc</th>
<th>Outcomesd</th>
<th>Duration of Follow-Up e</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ridner et al (2019)</td>
<td>1. Patient-reported outcomes not assessed</td>
<td>1. Patient-reported outcomes not assessed</td>
<td>1. Patient-reported outcomes not assessed</td>
<td>1. Patient-reported outcomes not assessed</td>
<td>1. Patient-reported outcomes not assessed</td>
</tr>
</tbody>
</table>

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

a 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.
b Intervention key: 1. Classification thresholds not defined; 2. Version used unclear; 3. Not intervention of interest.
c 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.
d 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).
e Follow-Up key: 1. Follow-up duration not sufficient with respect to natural history of disease (true-positives, true-negatives, false-positives, false-negatives cannot be determined).
Table 6. Study Design and Conduct Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection</th>
<th>Blinding</th>
<th>Delivery of Test</th>
<th>Selective Reporting</th>
<th>Data Completeness</th>
<th>Statistical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ridner et al (2019)</td>
<td>1. Open-label</td>
<td>2. 10 patients who progressed prior to triggered intervention were excluded</td>
<td>1. Confidence intervals not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

a Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).
b Blinding key: 1. Not blinded to results of reference or other comparator tests.
c 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.
e 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.
f 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. 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, but no preoperative measurements (no preoperative group). The authors compared the demographic and clinical characteristics of the preoperative and control groups and the preoperative and postoperative groups; they did not identify any statistically significant differences.

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.\textsuperscript{10,11,12,13,14,15,16,17,18} 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: Clinically Useful**

Interim results from an ongoing RCT comparing bioimpedance with standard tape measure following treatment for breast cancer have been published. Overall, 109 of 508 (21.5%) patients received early treatment due to reaching a pre-determined threshold to trigger an intervention. A total of 12 triggering patients progressed to clinical lymphedema (2 in the bioimpedance group [4.9%] and 10 in the tape measure group [14.7%]; \(P=0.130\)). The RCT was limited by its open-label design and lack of reporting of important health outcomes. One prospective comparative study has compared rates of clinical lymphedema in women managed with and without bioimpedance analysis. This study had several limitations, including nonrandomized design, lack of blinding, lack of complete data on a substantial proportion of enrolled patients, and lack of a systematic method for diagnosing lymphedema in the control group. The authors reported a significantly lower rate of clinical lymphedema in patients managed with bioimpedance analysis and who received treatment for subclinical lymphedema. An additional retrospective analysis suggested that postoperative bioimpedance monitoring is feasible but provided limited information on its efficacy. Additional studies to confirm these findings are needed, especially RCTs and trials that include an alternative method for early or subclinical lymphedema detection.

**Summary of Evidence**

For individuals who have known or suspected lymphedema who receive bioimpedance spectroscopy, the evidence includes a systematic review, one RCT, one prospective comparative observational study, and multiple uncontrolled observational studies. The relevant outcomes are test validity, symptoms, and quality of life. Diagnostic accuracy studies have found a poor correlation between bioimpedance analysis and the reference standard (volume displacement or circumferential measurement). Interim results from an ongoing RCT comparing bioimpedance with standard tape measure following treatment for breast cancer have been published. Overall, 109 of 508 (21.5%) patients received early treatment due to reaching a pre-determined threshold to trigger an intervention. A total of 12 triggering patients progressed to clinical lymphedema (2 in the bioimpedance group [4.9%] and 10 in the tape measure group [14.7%]; \(P=0.130\)). The RCT was limited by its open-label design and lack of reporting of important health outcomes. The single prospective comparative study found a significantly lower rate of clinical lymphedema in patients managed with bioimpedance devices but had several limitations, including nonrandomized design, lack of blinding, lack of complete data on a substantial proportion of enrolled patients, and lack of a systematic method for diagnosing lymphedema in the control group. Retrospective studies suggested that postoperative bioimpedance monitoring is feasible but provide limited information about its
efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

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
National Comprehensive Cancer Network Clinical Practice Guidelines on Survivorship (v.2.2019)\textsuperscript{19}, and Breast Cancer (v.3.2019)\textsuperscript{19}, recommend education, monitoring, and referral for lymphedema management as needed. Neither guideline mentions bioimpedance.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 7.

Table 7. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT03978754</td>
<td>Assessment of Breast Cancer-Related Arm Lymphedema—Comparison of Traditional Measurement Methods and Indocyanine Greeni¼“ICGi¼‰Lymphography</td>
<td>300</td>
<td>Jun 2019</td>
</tr>
<tr>
<td>NCT Number</td>
<td>Study Title</td>
<td>Enrollment</td>
<td>Study Start</td>
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<td>------------</td>
<td>------------------------------------------------------------------------------</td>
<td>------------</td>
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</tr>
<tr>
<td>NCT02743858</td>
<td>A Prospective Surveillance Program for Assessment and Treatment of Breast Cancer-Related Lymphedema After Axillary Lymph Node Dissection</td>
<td>850</td>
<td>Apr 2021</td>
</tr>
<tr>
<td>NCT01544335</td>
<td>Evaluation of the Validity of BIS as a Tool for Quantification of Lymphedema Through Comparison With Perometry and Self-Report</td>
<td>200</td>
<td>Sep 2020</td>
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<tr>
<td>Unpublished</td>
<td>Early Detection of Lymphedema With Bio-Electrical Impedance Analysis in Patients After Breast Cancer Surgery</td>
<td>60</td>
<td>Nov 2019</td>
</tr>
</tbody>
</table>

BIS: bioimpedance spectroscopy; NCT: national clinical trial.

REFERENCES
13. Whitworth PW, Cooper A. Reducing chronic breast cancer-related lymphedema utilizing a program of prospective surveillance with bioimpedance spectroscopy. Breast J. 2018 Jan;24(1). PMID 29063664


**Billing Coding/Physician Documentation Information**

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<td>93702</td>
<td>Bioimpedance spectroscopy (BIS), extracellular fluid analysis for lymphedema assessment(s)</td>
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**ICD10 Codes:**

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<td>I97.2</td>
<td>Postmastectomy lymphedema syndrome</td>
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<td>Z90.10</td>
<td>Acquired absence of breast and nipple code range</td>
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<td>Z90.13</td>
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Prior to 1/1/11, this service is likely being coded using CPT code 38999 – unlisted procedure, hemic or lymphatic system.

**Additional Policy Key Words**

N/A

**Policy Implementation/Update Information**

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<td>5/4/14</td>
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State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.