Bioimpedance Devices for Detection and Management of Lymphedema

Policy Number: 2.01.82  Last Review: 5/2018

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>With known or</td>
<td>Bioimpedance spectroscopy</td>
<td>Volume displacement</td>
<td>Test accuracy</td>
</tr>
<tr>
<td>suspected lymphedema</td>
<td></td>
<td>Circumferential measurement</td>
<td>Test validity</td>
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<td></td>
<td></td>
<td></td>
<td>Symptoms</td>
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<td>Quality of life</td>
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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 several prospective studies on diagnostic accuracy and a controlled observational study evaluating clinical utility. Relevant outcomes are test accuracy and validity, symptoms, and quality of life. Recent diagnostic accuracy studies have found a poor correlation between bioimpedance analysis and the reference standard (volume displacement or circumferential measurement). There are no randomized controlled trials evaluating the clinical utility of bioimpedance devices in the management of patients with lymphedema or at high risk of developing lymphedema. The single prospective comparative study found a significantly lower rate of clinical lymphedema in patients managed with bioimpedance devices. Limitations of this study included its retrospective design, lack of randomization or blinding, and lack of a systematic method for detecting early or subclinical lymphedema in the control group. An additional retrospective analysis suggested that postoperative bioimpedance monitoring is feasible, but provides limited information about its efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Background**

**Lymphedema**

Lymphedema is a chronic accumulation of fluid and fibrous tissue that results from the disruption of lymphatic drainage. Secondary lymphedema of the upper extremity may develop following surgery for breast cancer; it has been reported in approximately 25% to 50% of women following mastectomy. Lymphedema can be a disfiguring condition. It results from lymphatic dysfunction or disruption and can be difficult to diagnose and manage accurately. At least 1 systematic review has found that early detection of secondary lymphedema in breast cancer improves outcomes. One challenge is identifying the clinically significant limb swelling through simple noninvasive methods. Many techniques have been used for documenting lymphedema including measuring differences in limb volume (volume displacement) and limb circumference.

The detection of subclinical lymphedema (ie, the early detection of lymphedema before clinical symptoms become apparent) is another area of study. Detection of subclinical lymphedema (referred to as stage 0 lymphedema) is problematic. The subclinical disease may exist for months or years before overt edema is noted. This approach generally involves comparison of preoperative (ie, baseline) with postoperative measurements, because existing differences between upper extremities (like the effects of a dominant extremity) may obscure subtle differences resulting from the initial accumulation of fluid.
**Diagnosis**
Bioimpedance spectroscopy is based on the theory that the level of opposition to 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 U.S. Food and Drug Administration through the 510(k) process to aid in the assessment of lymphedema are summarized in Table 1.

**Table 1. Food and Drug Administration–Cleared Bioimpedance Spectroscopy Devices for Lymphedema**

<table>
<thead>
<tr>
<th>Year</th>
<th>Device</th>
<th>Manufacturer</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>MoistureMeterD</td>
<td>Delfin Technologies (Stamford, CT)</td>
<td>To aid informing a clinical judgment of unilateral lymphedema in women</td>
</tr>
<tr>
<td>2007</td>
<td>ImpediMed L-Dex™ U400</td>
<td>ImpediMed (Carlsbad, CA)</td>
<td>To aid clinical assessment of unilateral lymphedema of the arms in women</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 15, 2017.

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

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

The following PICOTS were used to select literature to inform this review.

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

Interventions
The relevant intervention of interest is bioimpedance spectroscopy.

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

Outcomes
The general outcomes of interest are test accuracy and validity, symptoms, and quality of life.

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

Setting
During a physical exam conducted by a physician in an inpatient or outpatient setting.

Simplifying Test Terms
There are 3 core characteristics for assessing a medical test. Whether imaging, laboratory, or other, all medical tests must be:

- Technically reliable
- Clinically valid
- Clinically useful.

Because different specialties may use different terms for the same concept, we are highlighting the core characteristics. The core characteristics also apply to different uses of tests, such as diagnosis, prognosis, and monitoring treatment.

Diagnostic tests detect presence or absence of a condition. Surveillance and treatment monitoring are essentially diagnostic tests over a time frame.
Surveillance to see whether a condition develops or progresses is a type of detection. Treatment monitoring is also a type of detection because the purpose is to see if treatment is associated with the disappearance, regression, or progression of the condition.

Prognostic tests predict the risk of developing a condition in the future. Tests to predict response to therapy are also prognostic. Response to therapy is a type of condition and can be either a beneficial response or adverse response. The term predictive test is often used to refer to response to therapy. To simplify terms, we use prognostic to refer both to predicting a future condition or to predicting a response to therapy.

**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 the 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).

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. The AHRQ assessment identified 8 studies that reported the sensitivity and specificity of tests to diagnose secondary lymphedema. Reviewers noted that 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 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.

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 2015 study by Barrio et al 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 a 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 a 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 a randomized controlled trial comparing health outcomes in patients managed with and without the use of bioimpedance devices. No randomized controlled trials were identified. However, a controlled observational study has compared clinical lymphedema rates in patients managed with and without bioimpedance analysis. This 2014 study, by Soran et al, 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.

Laidley et al (2016), in a retrospective cohort study conducted at 2 surgical practices, reported on the feasibility and outcomes for postoperative bioimpedance monitoring in women following axillary lymph node surgery for breast cancer. Of 1113 patients, 326 patients who had undergone some form of axillary staging and preoperative and at least 2 postoperative bioimpedance measurements met the study’s eligibility criteria. The cumulative incidence of subclinical breast cancer–related lymphedema was 12.3%.

**Section Summary: Clinically Useful**

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 randomized controlled trials 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 several prospective studies on diagnostic accuracy and a controlled observational study evaluating clinical utility. Relevant outcomes are test accuracy and validity, symptoms, and quality of life. Recent diagnostic accuracy studies have found a poor correlation between bioimpedance analysis and the reference standard (volume displacement or
circumferential measurement). There are no randomized controlled trials evaluating the clinical utility of bioimpedance devices in the management of patients with lymphedema or at high risk of developing lymphedema. The single prospective comparative study found a significantly lower rate of clinical lymphedema in patients managed with bioimpedance devices. Limitations of this study included its retrospective design, lack of randomization or blinding, and lack of a systematic method for detecting early or subclinical lymphedema in the control group. An additional retrospective analysis suggested that postoperative bioimpedance monitoring is feasible, but provides 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 with 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 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
No relevant guidelines or statements were identified.

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
A search of ClinicalTrials.gov in November 2017 did not identify any ongoing or unpublished trials that would likely influence this review.
References

Billing Coding/Physician Documentation Information
93702  Bioimpedance spectroscopy (BIS), extracellular fluid analysis for lymphedema assessment(s)

ICD10 Codes:
I97.2  Postmastectomy lymphedema syndrome
Z90.10-  Acquired absence of breast and nipple code range
Z90.13

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
1/1/11  New policy; considered investigational.
5/1/11  No policy statement changes.
5/1/12  No policy statement changes.
5/1/13  No policy statement changes.
5/4/14  Title changed to “Bioimpedance devices for detection and management of lymphedema”.
5/1/15  No policy statement changes.
5/1/16  No policy statement changes.
5/1/17  No policy statement changes.
5/1/18  No policy statement changes.
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.