Bioimpedance Devices for Detection and Management of Lymphedema

Policy Number: 2.01.82  Last Review: 5/2014

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.

Description of Procedure or Service
Secondary lymphedema may develop following surgery for breast cancer. Bioelectrical impedance is being studied as a diagnostic test for lymphedema, particularly for subclinical disease.

Background
Secondary lymphedema of the upper extremity may develop following surgical treatment for breast cancer; it has been reported in approximately 25 to 50% of women following mastectomy. This can be a chronic, disfiguring condition. It results from lymphatic dysfunction or disruption and can be difficult to accurately diagnose and manage. One challenge is identifying the presence of 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. A number of newer techniques are being evaluated, including bioimpedance with use of bioimpedance spectroscopy (BIS) analysis, which uses resistance to electrical current in comparing the composition of fluid compartments. BIS is based on the theory that the amount 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.

The detection of subclinical lymphedema; that is, 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. Subclinical disease may exist for months or years before overt edema is noted. This approach generally involves comparison of preoperative with postoperative measurements, since existing differences between upper extremities (like the effects of a dominant extremity) may obscure early, subtle differences resulting from the initial accumulation of fluid. Bioimpedance has been proposed as one diagnostic test for this condition. Those who support the approach to diagnose subclinical disease believe that early treatment of subclinical lymphedema should result in less severe chronic disease.

Regulatory Status
One of the devices is the ImpediMed L-Dex™ U400 cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process in 2007 (1) and in 2008 (2). According to the FDA letter, the device is “to aid in the clinical assessment of unilateral lymphedema of the arm in women. The device is not intended to diagnose or predict lymphedema of an extremity.”

Rationale

Assessment of a diagnostic technology typically focuses on 3 parameters: (1) technical performance; (2) diagnostic performance (sensitivity, specificity, and positive and negative predictive value) in appropriate populations of patients; and (3) demonstration that the diagnostic information can be used to improve patient outcomes (clinical utility). While in some cases, tests can be adequately evaluated using technical and diagnostic performance, when a test identifies a new or different group of patients with a disease, randomized controlled trials (RCTs) are needed to demonstrate impact of the test on the net health outcome.

Literature Review

When the policy was created, a literature search was conducted using MEDLINE through January 2010 to identify relevant studies. The policy was updated regularly with MEDLINE searches, most recently for the period September 2012 through October 11, 2013.

Technical performance

Technical performance of a device is typically assessed with 2 types of studies, those that compare test measurements with a gold standard and those that compare results taken with the same device on different occasions (test-retest). While there is no absolute gold standard for diagnosis of lymphedema, the de facto gold standards are limb volume and/or limb circumference. Studies that address technical performance of bioimpedance devices are described below:

A 2010 publication by Czerniec et al. reported on measurement of lymphedema in a small group of patients, 33 with lymphedema and 18 without. (1) This study was to determine the relationship between physical methods of measuring lymphedema and self-reported swelling. Measurement techniques included self-report, bioimpedance spectroscopy, perometer, and the truncated cone method. The authors noted that the physical measurement tools were highly reliable with high concordance (0.89 to 0.99, respectively). In this study, self-report correlated moderately with physical measurements (0.65 to 0.71, respectively) and was moderately reliable. The authors concluded that lymphedema assessment methods are concordant and reliable but not interchangeable.

In a U.S.-based study published in 2007, Warren and colleagues evaluated 15 patients with upper- or lower-extremity secondary lymphedema documented by lymphoscintigraphy, along with 7 healthy controls using bioimpedance spectroscopy (BIS) analysis. (2) In addition, both the affected and unaffected limbs in lymphedema patients were evaluated so patients also served as their own controls. According to BIS in the lymphedema patients, the average ratio of current flow of the affected limb to the unaffected limb (the impedance ratio) was 0.9 (range, 0.67 to 1.01). In the control group, the average impedance ratio was 0.99 (range, 0.95 to 1.02). Lower impedance ratio values correlated with higher levels of accumulated fluid.

Diagnostic performance

A technology assessment on the diagnosis and treatment of secondary lymphedema, performed under contract from Agency for Healthcare Research and Quality (AHRQ) by the McMaster University Evidence-based Practice Center, was released in May 2010. (3) The assessment identified 8 studies that reported the sensitivity and specificity of tests to diagnose secondary lymphedema. Two of these studies evaluated bioimpedance devices, Cornish et al. 2001 (4) and Hayes et al. 2008, (5) and are briefly described below:
Cornish et al. in Australia followed 102 patients after treatment for breast cancer. (4) Twenty patients developed lymphedema in the 24-months follow-up period, and in these 20 cases, multifrequency bioelectrical impedance analysis (MFBIA) predicted the onset of the condition up to 10 months before the condition was diagnosed clinically. Estimates of the sensitivity and specificity were both approximately 100%. At the time of detection by MFBIA, only one of the patients had a positive test result from the total limb volume determined from the circumferential measures.

In another study from Australia, Hayes et al. noted that the point prevalence of lymphedema varies according to the approach to diagnosis. (5) In this study, lymphedema status was assessed at 3-month intervals between 6 and 18 months postsurgery in a sample of Australian women with unilateral, invasive breast cancer, using 3 methods: bioimpedance spectroscopy, difference between sum of arm circumferences (SOAC), and self-report. Depending on the method, point prevalence ranged between 8% and 28%, with 1 in 5 to 2 in 5 women experiencing lymphedema at some point in time. According to the technology assessment, the sensitivity and specificity of bioimpedance compared to SOAC was 42% and 88%, respectively and the sensitivity and specificity of bioimpedance compared to self-report was 61% and 59%, respectively.

More recently, in 2011, Smoot et al. reported on diagnostic test characteristics including sensitivity, specificity, and area under the receiver-operating-characteristic (ROC) curve for a number of tests used in the diagnosis of breast cancer-related lymphedema. (6) For this study, a total of 141 women were classified as having (n=70) or not having (n=71) breast cancer-related lymphedema (BCRL) based on past diagnosis by a healthcare provider. Areas under the curve for a number of bioimpedance measures and volume measures were in the 0.79 to 0.88 range, with overlap in confidence intervals. Given questions about the standard used for diagnosis and apparent lack of patients with subclinical lymphedema, this study provides little new information. Finally, in a study from Australia, Ward and colleagues concluded that the impedance ratio thresholds for early detection of lymphedema remain suitable for clinical use with present-day analyzers. (7)

In 2012, Vicini et al. published a retrospective analysis of data from 64 women who underwent surgery for breast cancer and had pre- and postsurgical measurements of bioelectrical impedance assessment using an ImpediMed L-Dex device. (8) Postsurgical measurement occurred within 90 days of surgery and before radiation therapy or chemotherapy. Change in the lymphedema index ratios (LIR) pre- and postprocedure was compared. LIR was defined as the difference in volume or impedance between the affected and nonaffected arm. The authors did not discuss a reference standard test. For the group as a whole, median LIR was 0.5 at baseline and the median change in LIR after surgery was 1.1. The authors noted that, although differences between groups were not statistically significant, there appeared to be a greater change in LIR pre- and postsurgery in patients who received more aggressive treatment e.g., larger numbers of nodes removed or dissection of axillary nodes compared to sentinel node only. The study did not include a reference standard test and did not report sensitivity and specificity of bioelectrical impedance analysis.

Clinical utility

The ideal study design is a randomized controlled trial (RCT) comparing health outcomes in patients who were managed with and without the use of bioimpedance devices; no studies of this type were identified.

A related question is whether early detection and treatment of subclinical lymphedema, using a bioimpedance device or another detection method, improves health outcomes. The literature on treatment shows variability among studies regarding response to therapy for secondary lymphedema. Some studies found that mild disease was more responsive to treatment; other studies did not. Similarly, when duration of symptoms was reported, there was no clear relationship between duration of the edema and response to treatment.
A study by Stout Gergich et al., published in 2008, is frequently cited as support for the early detection and treatment of subclinical lymphedema. In this study, lymphedema was identified in 43 of 196 women who participated in a prospective breast cancer morbidity trial. Limb volume was measured preoperatively and at 3-month intervals after surgery using perimetry (another evolving technique). If an increase of greater than 3% in upper limb volume developed compared with the preoperative volume, a diagnosis of lymphedema was made and a compression garment intervention was prescribed for 4 weeks. Statistical analysis was a repeated-measures analysis of variance by time and limb \( (p \leq 0.001) \) comparing the lymphedema cohort with an age-matched control group. In this study, the time to onset of lymphedema averaged 6.9 months postoperatively. The mean (± standard deviation) affected limb volume increase was 83 mL (±119) at lymphedema onset compared with baseline. Of note, clinical lymphedema is generally felt to be apparent when 200 mL of fluid accumulates. After the intervention, a statistically significant mean 48 mL (±103) volume decrease was realized. The mean duration of the intervention was 4.4 weeks. Volume reduction was maintained at an average follow-up of 4.8 months after the intervention. The authors concluded that a short trial of compression garments effectively treated subclinical lymphedema. This study does not answer the key question; that is, whether net health outcome was improved by early intervention. In addition, the role of novel diagnostic testing compared to the use of the de facto gold standard tests (limb volume or circumference) also needs to be evaluated.

Another study on whether early detection and treatment of subclinical lymphedema improves health outcomes was published in 2009 by Boccardo et al. The study did not involve the use of bioimpedance devices so it cannot be considered evidence that their use improves outcomes. Fifty-five women were randomly assigned to a preventive intervention or control group. The preventive intervention consisted of volumetric (arm volume) measurements and early management of lymphedema once identified. Among the 49 of 55 women (89%) assessed at 2 years, the incidence of secondary lymphedema was 8% in the preventive group and 33% in controls. This is a relatively small study, and the various interventions used may have each played a role in the outcome for this study. Moreover, as noted earlier, the study did not include use of bioimpedance devices.

**Clinical Input Received through Physician Specialty Societies and Academic Medical Centers**

Clinical input on this policy was received from 2 academic medical centers and 2 specialty societies 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, who was from an academic medical center, thought that use of the technology is a reasonable alternative, especially in situations in which minor lymphedema can have a large impact on a patient. One specialty society noted that it supports support further research into effectiveness of this technology and recommends reimbursement in the context of relevant clinical trials.

**Summary**

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.

**Medicare National Coverage**

There is no national coverage determination on bioimpedance devices. In the absence of an NCD, coverage decisions are left to the discretion of the local Medicare carriers.

**References**

Billing Coding/Physician Documentation Information

0239T Bioimpedance spectroscopy (BIS), measuring 100 frequencies or greater, direct measurement of extracellular fluid differences between the limbs

Effective January 1, 2011, there is a specific CPT category III code for bioelectrical impedance testing (0239T):

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”.

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