Name of Policy:
Bioimpedance Devices for Detection of Lymphedema

Policy #: 438       Latest Review Date: November 2013
Category: Medicine       Policy Grade: C

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**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.

Secondary lymphedema of the upper extremity may develop following surgical treatment for breast cancer; it has been reported in about 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 differences in limb volume (volume displacement) and limb circumference measurements. 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 due to 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.

**Policy:**
**Devices using bioimpedance (bioelectrical impedance spectroscopy) do not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and are considered **investigational** for use in the diagnosis, surveillance, or treatment of patients with lymphedema, including use in subclinical secondary lymphedema.

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*Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.*
**Key Points:**
Assessment of a diagnostic technology typically focuses on three parameters: 1) its 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.

**Technical performance**
Technical performance of a device is typically assessed with two 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 and colleagues reported on measurement of lymphedema in a small group of patients, 33 with lymphedema and 18 without. 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 seven healthy controls using BIS analysis. 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. The assessment identified eight studies that reported the sensitivity and specificity of tests to diagnose secondary lymphedema. Two of these studies evaluated bioimpedance devices, Cornish et al. 2001 and Hayes et al. 2008, and are briefly described below:

Cornish and colleagues in Australia followed 102 patients after treatment for breast cancer. Twenty patients developed lymphedema in the 24 months’ follow-up period, and in these 20
cases, multi-frequency bioelectrical impedance analysis (MFBIA) predicted the onset of the condition up to ten 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 and colleagues noted that the point prevalence of lymphedema varies according to the approach to diagnosis. In this study, lymphedema status was assessed at three-month intervals between six and 18 months post-surgery in a sample of Australian women with unilateral, invasive breast cancer, using three methods: bioimpedance spectroscopy, difference between sum of arm circumferences (SOAC), and self-report. Depending on the method, point prevalence ranged between 8% to 28%, with one in five to two in five 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 and colleagues 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. 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.

In 2012, Vicini and colleagues published a retrospective analysis of data from 64 women who underwent surgery for breast cancer and had pre-surgical and post-surgical measurements of bioelectrical impedance assessment using an ImpediMed L-Dex device. Post-surgical measurement occurred within 90 days of surgery and before radiation therapy or chemotherapy. Change in the lymphedema index ratios (LIR) pre- and post-procedure was compared. LIR was defined as the difference in volume or impedance between the affected and non-affected 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 post-surgery 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 and colleagues, 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 three-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 four weeks. Statistical analysis was a repeated-measures analysis of variance by time and limb (p<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 [SD]) affected limb volume increase was 83 mL (+/-119 mL) 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 mL) 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 and colleagues. The study did not involve the use of bioimpedance devices so cannot 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 two 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.

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 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.

**Key Words:**
Bioelectrical impedance testing, Bioimpedance spectroscopy, Lymphedema, bioimpedance
testing, Bioimpedance analysis, BIS, Impedance plethysmography, Impedimed, LDex,
Plethysmography

**Approved by Governing Bodies:**
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 and in 2008. 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.”

**Benefit Application:**
Coverage is subject to member’s specific benefits. Group specific policy will supersede this
policy when applicable.

ITS: Home Policy provisions apply
FEP: Special benefit consideration may apply. Refer to member’s benefit plan. FEP does not
consider investigational if FDA approved. Will be reviewed for medical necessity.
Pre-certification requirements: Not applicable

**Current Coding:**
CPT Codes:

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<th>Code</th>
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| 0239T | Bioimpedance spectroscopy (BIS), measuring 100 frequencies or
greater, direct measurement of extracellular fluid differences
between the limbs (Effective for dates of service on or after
January 1, 2011) |

**Previous Coding:**
There are no specific codes for this procedure. (Deleted January 1, 2011)
References:

Policy History:
Medical Policy Group, June 2010 (3)
Medical Policy Administration Committee, July 2010
Available for comment July 2-August 16, 2010
Medical Policy Group, December 2010 – Added Code effective Jan 1, 2011
Medical Policy Group, April 2011: Added 2011 Update-Key Points, Updated References
Medical Policy Group, September 2012 (3): 2012 Update to Key Points & References
This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.