

Title	Reference	Authors	Year	Topic	Summary
<b>Early Detection and Treatment</b>					
The importance of detection of subclinical lymphedema for the prevention of breast cancer-related clinical lymphedema after axillary lymph node dissection; a prospective observational study.	Lymphat Res Biol 12(4): 289-294.	Soran, A., Ozmen, T. et al.	2014	Breast Ca	180 patients with breast cancer diagnosis and ALND. Comparison of 3 patient groups: (i) "Pre-op" - L-Dex pre-op and at follow-up (n=72), (ii) "Control" - L-Dex pre-op and only tape measure at follow-up (n=44) and (iii) "No pre-op" - no pre-op assessment L-Dex and tape measure at follow-up (n=64). Groups well matched but no randomization. Detection of LE in early subclinical phase and timely intervention led to a reduction in the incidence of clinical LE incidence from 36.4% to 4.4%.
Bioelectrical Impedance for Detecting and Monitoring Lymphedema in Patients with Breast Cancer. Preliminary Results of the Florence Nightingale Breast Study Group.	Lymphat Res Biol 2014 (Epub ahead of print)	Erdogan Iyigun, Z., et al.,	2014	Breast Ca	37 patients who underwent surgery for early-stage breast cancer were followed for lymphedema. L-Dex measures taken pre-op, 3, 6, 9 and 12 months post op. 8 patients (21.6%) were identified as having lymphedema, 3 at stage 0, 2 at stage 1 and 3 at stage 2. Intervention resulted in symptomatic improvement for all except one patient. This patients was identified at stage 1 and was non-compliant with therapy and progressed to stage 2. It was concluded that regular monitoring of high-risk patients improves treatment results.
The use of Bioimpedance Spectroscopy to Monitor Therapeutic Intervention in Patients Treated for Breast Cancer Related Lymphedema.	Lymphology 2013;46:184-92.	Shah C, Vicini F, Beisch P, et al.	2013	Breast Ca	Retrospective analysis of 50 patients comparing those that underwent BCRL treatment to those that did not. L-Dex scores significantly reduced in those treated and for those with elevated post-operative L-Dex scores, significant reduction with intervention as well. BIS able to detect early onset BCRL and observe treatment response.
Five Year Preliminary Outcomes of a Prospective Surveillance Model to Reduce Upper Extremity Morbidity Related to Breast Cancer Treatment.	San Antonio Breast Conference, 2011	Stout	2011	Breast Ca	5 year update, Stout 2008: Incidence of lymphedema was 7%-22% at 12 months and 11%-38% at 60 months. 12 month to 60 month comparison by stage: Stage 0: 22% vs 38%; Stage I/II: 7% vs 11%; Stage III: 0% vs 0%, respectively. Preliminary data demonstrates long term benefits for early subclinical treatment of patients. "Preoperative assessment, prospective surveillance, and early intervention enhance function and reduces morbidity. Early assessment and intervention should be the standard of care for patients receiving breast cancer treatment."
Arm lymphoedema in a cohort of breast cancer survivors 10 years after diagnosis.	Acta Oncol 2010;49:166-173	Johansson K, Branje E.	2010	Breast Ca	Retrospective study of 292 patient with breast cancer treated with ALND and RT. Those with BCRL were followed for up to 10 years (n=98) with water displacement and volumes kept at a low level throughout. Small volume at diagnosis important to prevent progression.
Effectiveness of early physiotherapy to prevent lymphoedema after surgery for breast cancer: randomised, single blinded, clinical trial.	BMJ 2010;340:b5396.	Torres Lacomba M, Yuste Sanchez MJ, Zapico Goni A, et al.	2010	Breast Ca	Randomized trial of 120 women with breast cancer treated with either early physiotherapy and education or education only. At one year, development of BCRL in 7% with interventions vs. 25% without (p=0.01), BCRL diagnosed 4 times more frequently.

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Time Course of Mild Arm Lymphedema After Breast Conservation Treatment for Early Stage Breast Cancer.	Int J Radiat Oncol Biol Phys 2010;76:85-90.	Bar Ad V, Cheville A, Solin LJ, et al.	2010	Breast Ca	Study of 109 patients with BCRL following BCT with mild arm edema (2 cm or less). Freedom from progression 79% at 1 year, 66% at 3 years, 52% at 5 years. Risk of progression even with low volumes.
Prospective Evaluation of a Prevention Protocol for Lymphedema following Surgery for Breast Cancer.	Lymphology 2009;42:1-9.	Boccardo FM, Ansaldi F, Belini C.	2009	Breast Ca	Randomized trial of 55 women with breast cancer undergoing ALND; patients were randomized to preventative protocol (lymphoscintigraphy, edema minimization protocol, and early management) or not. At 2 years, 8% developed BCRL (> 200 mL) as compared with 33% in the control group.
Preoperative assessment enables the early diagnosis and successful treatment of lymphedema.	Cancer 112(12): 2809-2819.	Stout Gergich, N. L., L. A. Pfalzer, et al.	2008	Breast Ca	Prospective trial of 196 patients, 43 of whom were identified to have BCRL. Compression sleeve given to those with 3% or greater increase in volume (perometry) for 4 weeks. Time to onset 6.9 months post-operatively with intervention associated with a 48 mL reduction that was maintained after intervention. "In conclusion, preoperative assessment in the context of a prospective surveillance model enables the early detection and management of subclinical LE. An early intervention protocol with 20- to 30-mm Hg compression garments, as outlined in this report, significantly reduces the affected limb volume to near baseline measures and prevents progression to a more advanced stage of LE for at least the first year postoperatively."
Lymphoedema secondary to breast cancer: Possibility of diagnostic and therapeutic prevention.	Ann Ital Chir 2002;73:493-8.	Campisi BC, Boccardo F, Zill A, et al.	2002	Breast Ca	Randomized trial of 50 women with breast cancer randomizing patients to lymphoscintigraphy or normal clinical follow up. Those with lymphoscintigraphy abnormalities provided treatment prior to clinical BCRL development. Subsequent development of clinically evident BCRL in 8% vs. 36% in control group.
Edema Volume, Not Timing, is the Key to Success in Lymphedema Treatment.	Am J Surg 1999;178:311-5.	Ramos SM, O'Donnell LS, Knight G.	1999	Breast Ca	69 patients were analyzed for response to decongestive therapy with little correlations shown between duration and volume or duration and response to treatment. However, initial volume corresponds with response. Less than 250 ml leads to 78% reduction vs. 56% with 250-500 ml.

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<b>Implementation/Feasibility</b>					
Bioelectrical impedance self-measurement protocol development and daily variation between healthy volunteers and breast cancer survivors with lymphedema.	Lymphat Res Biol 2014;12:2-9.	Ridner SH, Bonner CM, Doersam JK, et al.	2014	Breast Ca	Pilot study demonstrates feasibility of incorporating home self assessment with BIS.
Bioelectrical Impedance for Detecting and Monitoring Patients for the Development of Upper Limb Lymphedema in the Clinic.	Clin Breast Cancer 2012;12:133-7.	Vicini F, Shah C, Lyden, M, et al.	2012	Breast Ca	Study of 64 patients evaluated with BIS. Provides information on implementation of BIS into clinic and demonstrates feasibility of utilizing BIS to make clinical decisions based on aggressiveness of locoregional therapy.
Bioimpedance Analysis in the Assessment of Lymphoedema Diagnosis and Management.	Journal of Lymphoedema 2007;2:44-8.	Rockson SG.	2007	Generic	MFBIA (BIS) in analysis of lymphedema has been proven to be fast, accurate and well accepted by patients. Will provide good standard for lymphedema detection and tracking.

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<b>Diagnostic Comparison</b>					
L-Dex ratio in detecting breast cancer-related lymphedema: reliability, sensitivity, and specificity.	Lymphology 2013;46:85-96.	Fu MR, Cleland CM, Guth AA, et al.	2013	Breast Ca	Study of 250 women including healthy patients, patients with BCRL, and those at risk to develop BCRL. Bioimpedance found to be reliable in healthy women, those at risk and those with BCRL. Correlated with limb circumference.
Determining the precision of dual energy x-ray absorptiometry and bioelectric impedance spectroscopy in the assessment of breast cancer-related lymphedema.	Lymphat Res Biol 2013;11:104-9.	Newman AL, Rosenthal L, Towers A, et al.	2013	Breast Ca	Study of 24 women with BCRL. Compared DXA and BIS and found both to be precise in measuring lean mass, fat mass, and ECF volume.
Does the Effect of Weight Lifting on Lymphedema Following Breast Cancer Differ by Diagnostic Method; Results of a Randomized Controlled Trial.	Breast Cancer Res Treat 2011;130:227-34.	Hayes SC, Speck RM, Reimet E, et al.	2011	Breast Ca	Randomized trial of 295 women with breast cancer comparing 4 diagnostic techniques (water displacement, circumference, BIS, and survey) and comparing weight lifting intervention vs. no weight lifting. BCRL diagnosis varied between 22% and 52%, highlighting difference in sensitivity of diagnostic modalities.
Comparison of Diagnostic Accuracy of Clinical Measure of Breast Cancer Related Lymphedema: Area Under the Curve.	Arch Phys Med Rehabil 2011;92:603-10.	Smoot BJ, Wong JF, Dodd MJ.	2011	Breast Ca	Cross-sectional study of women with chronic BCRL (n=70) and no BCRL (n=71). Comparison of past diagnosis by physician and alternative diagnostic techniques. BIS yielded the highest accuracy based on AUC curves in assessing existing BCRL.
Correlation between Bioelectrical Spectroscopy and Perometry in Assessment of Upper Extremity Swelling.	Lymphology 2010;43:85-94.	Jain MS, Danoff JV, Paul SM.	2010	Breast Ca	Study of 10 women treated for breast cancer and found that BIS had high inter and intra-rater reliability and concurrent validity as compared with perometry.
Assessment of Breast Cancer-Related Arm Lymphedema—Comparison of Physical Measurement Methods and Self-Report.	Cancer Invest 2010;28:54-62.	Czerniec SA, Ward LC, Regshaug KM, et al.	2010	Breast Ca	Study of 51 women, 33 with BCRL and 18 without, examining diagnostic methods (BIS, perometry, self-report, truncated cone). Reliability between methods except self report. However, techniques were not interchangeable. BIS found to be highly reliable.
Segmental measurement of breast cancer-related arm lymphoedema using perometry and bioimpedance spectroscopy.	Support Care Center 2011;19:703-10.	Czerniec SA, Ward LC, Lee MJ, et al.	2010	Breast Ca	Study of 40 women, 29 with BCRL and 11 without with measurements taken with BIS and perometry. BIS able to detect higher inter-limb ratios than perometry in women lymphedema but not without. Increased sensitivity with BIS.
Operational Equivalence of Bioimpedance Indices and Perometry for the Assessment of Unilateral Arm Lymphedema.	Lymphat Res Biol 2009;7:81-5.	Ward LC, Czerniec S, Kilbreath SL.	2009	Breast Ca	Study measured impedance in 45 women with BCRL and 21 without and also evaluated volume with perometry. Impedance ratios correlated with perometry volumes.

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Quantitative bioimpedance spectroscopy for the assessment of lymphoedema.	Breast Cancer Res Treat 2009;117:541-7.	Ward LC, Czerniec S, Kilbreath SL.	2009	Breast Ca	Control cohort of women (n=69) utilized to predict arm volumes in women with lymphedema (n=23) and those without (n=13) with comparison to perometry. Arm volumes correlated with those predicted by BIS, with no significant difference in arm size prediction and that measured by BIS. Increase in fluid associated with increase in ECF primarily (60%). This observation concurs with the accepted course of progression of lymphoedema in which the earliest events include accumulation of lymph, an extracellular fluid. The inference can also be drawn that BIS is better suited for monitoring early stage lymphedema, where changes are predominantly in fluid volume.
Reliability of Bioimpedance Spectroscopy and Tonometry after Breast Conserving Cancer Treatment.	Lymph Res Biol 2008;6:85-7.	Moseley A, Piller N.	2008	Breast Ca	Study of 14 women with breast cancer evaluating reproducibility of tonometry and BIS. Found that the both were reliable and allowed for early detection of fluid increases.
Lymphedema secondary to breast cancer: how choice of measure influences diagnosis, prevalence, and identifiable risk factors.	Lymphology 2008;41:18-28.	Hayes S, Janda M, Cornish B, et al.	2008	Breast Ca	Study of 287 women comparing of different diagnostic techniques (BIS, circumference, self-report) used to identify prevalence/cumulative burden of BCRL following treatment. Difference in prevalence noted by method with 40-60% of cases undetected by circumference or survey that were identified with BIS. Compared with BIS, circumferential measurements had 42% sensitivity and 88% specificity for detection of lymphedema. For self-assessment, the sensitivity was 61% and the specificity was 59%.
Bioelectrical Impedance Analysis: Proven Utility in Lymphedema Risk Assessment and Therapeutic Monitoring.	Lymphat Res Biol 2006;4:51-6.	Ward LC.	2006	Breast Ca	Variation of repeated assessments (same day) (Average $\pm$ Std Dev) - Lymphometer (Bioimpedance ECW ratio): 0.60 $\pm$ 15.4%; Tape measure ratio: 2.1 $\pm$ 35%; Arm Volume (Tape) : 1.4 $\pm$ 31%; Bioelectric impedance measurements using the Lymphometer were: 1) Faster, 2) Better accepted by nursing personnel, 3) More consistent than either serial tape measurements or water displacement methods.
Comparison of methods to diagnose lymphoedema among breast cancer survivors: 6-month follow-up.	Breast Cancer Res Treat 2005;89:221-6.	Hayes S, Cornish B, Newman B.	2005	Breast Ca	Study of 176 women with breast cancer to compare diagnostic modalities (BIS, circumference, survey) to identify BCRL. Of those identified by BIS, only 35% identified by circumference and 65% by survey.
Bioelectrical impedance for monitoring the efficacy of lymphoedema treatment programmes.	Breast Cancer Res Treat 1996;38:169-76.	Cornish BH, Bunce IH, Ward LC, et al.	1996	Breast Ca	Study of 20 patients with breast cancer and 20 healthy controls assessed with multifrequency bioimpedance. Demonstrate increased sensitivity with MFBIA as compared with circumference standard.

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<b>Validation Studies</b>					
Comparing Bioelectrical Impedance Values in Assessing Early Upper Limb Lymphedema after Breast Cancer Surgery.	In Vivo 2012;26:863-7.	Berlit S, Brade J, Tuschy B, et al.	2012	Breast Ca	Whole body bioimpedance for 33 women treated for breast cancer. Found good sensitivity and specificity along with high negative predictive value.
Confirmation of the Reference Impedance Ratios Used for Assessment of Breast Cancer-Related Lymphedema by Bioelectrical Impedance Spectroscopy.	Lymphat Res Biol 2011;9:47-51.	Ward LC, Dylke E, Czerniec S, et al.	2011	Breast Ca	Study of 172 healthy females indicates that impedance ratio thresholds are consistent with those previously identified.
Bioimpedance in the assessment of unilateral lymphedema of a limb: the optimal frequency.	Lymphat Res Biol 2011;9:93-9.	Gaw R, Box R, Cornish B.	2011	Generic	Studied limb impedance in healthy cohort as well as those with upper and lower extremity edema. Found good differentiation between the arm and leg L-Dex measured for lymphedema subjects and the arm and leg L-Dex measured for control subjects up to a frequency of about 30 kHz. Concludes that impedance measurements above a frequency of 30 kHz decrease sensitivity to extracellular fluid and are not reliable for early detection of lymphedema. (The FDA cleared BIS device calculates impedance ratios based on an optimal 0 kHz frequency.)
Bioelectrical Impedance for Detecting Upper Limb Lymphedema in Nonlaboratory Settings.	Lymphat Res Biol 2009;7:11-5.	Ridner SH, Dietrich MS, Deng J, et al.	2009	Breast Ca	Study evaluating impedance ratios using single frequency impedance in healthy women, patients with BCRL, and patients with breast cancer without BCRL. Control and non-BCRL similar while BCRL patients significantly different ratios.
The Use of Bioimpedance Analysis to Evaluate Lymphedema.	Ann Plast Surg 2007;58:541-3.	Warren AG, Janz BA, Slavin SA, et al.	2007	Generic	Study of 15 patients with upper or lower extremity edema as noted by lymphoscintigraphy and 7 healthy volunteers using multifrequency bioimpedance (BIS). Found that BIS can be used to identify edema in either upper and lower extremities and is quick and reproducible.
A new detection technique for lymphedema with application in both unilateral and bilateral cases.	Angiology 2002;53:41-7.	Cornish BH, Thomas BJ, Ward LC, et al.	2002	Generic	Study of 20 patients using multifrequency bioimpedance to identify lymphedema index without contralateral control. Results confirmed that the established techniques of total limb volume and extracellular fluid volume normalized to the unaffected contralateral limb were accurate in the detection of lymphedema.
Early diagnosis of lymphedema using MFBI.	Lymphology 2001;34:2-11.	Cornish BH, Chapman M, Hirst C, et al.	2001	Breast Ca	Prospective study of 102 patients with breast cancer and 60 healthy controls. Healthy subjects used to identify normal range of ratio (dominant/non-dominant). 20 patients developed BCRL with multifrequency bioimpedance identifying this up to 10 months(mean 4 months) prior. Sensitivity and Specificity 100% and 98% while circumference tape had a 5% sensitivity.
Use of Bioimpedance Spectroscopy to determine extracellular fluid, intracellular fluid, total body water, fat mass and fat-free mass.	Basic Life Sci 1993;60:67-70.	Van Loan MD, Withers P, Matthie J, et al.	1993	Generic	Extracellular fluid was determined by NaBr dilution (reference method). Tests against a known electronic circuit resulted in accuracy of +/-1%. Test-retest in human subjects showed no significance difference with the reference method (p>0.41). Correlation with NaBr r=0.893. Concludes that BIS can be used successfully for the determination of body fluid compartments and is of potential use in a wide variety of clinical diseases.

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<b>Guidelines</b>					
National Lymphedema Network Position Papers	<a href="http://www.lymphnet.org/pdfDocs/nlnBCLE.pdf">http://www.lymphnet.org/pdfDocs/nlnBCLE.pdf</a>	National Lymphedema Network	2013	Breast Ca	Recommend reliable, reproducible assessment technique with standardized cut offs to initiate treatment. Bioelectrical spectroscopy (BIS) represents a reliable technique that can be used to detect early lymphedema.
Recent Advances in Breast Cancer Related Lymphedema Detection and Treatment: White Paper	<a href="http://www.avonfoundation.org/assets/le-meeting/le-white-">http://www.avonfoundation.org/assets/le-meeting/le-white-</a>	Avon Foundation for Women	2011	Breast Ca	Recognizes bioimpedance as a new technique that can be utilized for early detection. Notes BIS is validated and economical compared to alternatives used for early detection.

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<b>Economics/Quality of Life</b>					
Quality of life of women with lower limb swelling or lymphedema 3-5 years following endometrial cancer.	Gynecol Oncol 2014; 133(2): 314-8.	Rowlands IJ, Beesley VL, Janda M, et al.	2014	Legs	Survey of 1399 women with endometrial cancer. Those with lower limb lymphedema/swelling had reduced physical QOL 3-5 years following treatment.
Economic Benefits of BIS-Aided Assessment of post-BC Lymphedema in the United States.	Am J Manag Care 2012:234-41.	Billr SP, DeKoven MP, Munakata J.	2012	Breast Ca	Economic analysis demonstrating that BIS utilization would lead to a cost savings which is magnified when considering sequelae of BCRL.
Incidence, treatment costs, and complications of lymphedema after breast cancer among women of working age: a 2-Year follow-up study.	J Clin Oncol 2009;27:2007-14	Shih YC, Xu Y, Cormier JN, et al.	2009	Breast Ca	Claims study of 1,877 patients for 2 years after the start of cancer treatment. 10% of patients developed lymphedema with ALND and chemotherapy associated with development. Higher medical costs associated with BCRL diagnosis (\$23, 167 vs. \$14,877) with higher rates of cellulitis/lymphangitis noted.

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<b>Pathophysiology</b>					
Pathophysiology of lymphedema.	Semin Oncol Nurs 2013;29:4-11.	Ridner SH.	2013	Generic	Lymphedema pathophysiology overview and implications.
Current concepts and future directions in the diagnosis and management of lymphatic vascular disease.	Vasc Med 2010;15:223-31.	Rockson SG.	2010	Generic	A review of lymphatic biology, pathology and evolving concepts about the diagnostic and therapeutic approaches based on the relevant fluid changes.
The pathophysiology of lymphedema.	Cancer 1998;83:2798-802.	Mortimer PS.	1998	Generic	Edema represents an increase in interstitial fluid volume sufficient to manifest with swelling. Any edema, whatever the underlying cause, is due to an imbalance between capillary filtration and lymph drainage.

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<b>Review Articles</b>					
Cancer-Related Lymphedema Risk Factors, Diagnosis, Treatment, and Impact: A Review.	J Clin Oncol 2012;30:3726-33.	Paskett ED, Dean JA, Oliveri JM, et al.	2012	Generic	Review of cancer-related lymphedema with identification of bioimpedance as an emerging diagnostic technique with greater ease and comfort than traditional diagnostics. Notes that lymphedema can significantly impair QOL.
Breast Cancer Related Arm Lymphedema: Incidence Rates, Diagnostic Techniques, Optimal Management and Risk Reduction Strategies.	Int J Radiat Oncol Biol Phys 2011;81:907-14.	Shah C, Vicini FA.	2011	Breast Ca	"Traditional measures use total arm volume as a surrogate for LE (lymphedema). However, this is not completely accurate because LE represents an increase in the extracellular fluid volume. ....newer modalities can directly measure the extracellular volume, potentially providing increased diagnostic accuracy... Newer diagnosis techniques including DEXA and BIS represent significant improvements over traditional techniques by providing standardized cutoffs, limiting observer variability, increasing sensitivity with the potential of subclinical detection, and accurately measuring the extracellular fluid space."
Lymphedema: How Do We Diagnose and Reduce the Risk of This Dreaded Complication of Breast Cancer Treatment?	Current Breast Cancer Reports 2010; 2:53-58	Bernas MJ, Askew RL, Armer JM, et al.	2010	Breast Ca	Encourages healthcare providers involved with cancer patients to become more educated about lymphedema, aware of current risk-reduction practices, and familiar with methods of diagnosis and assessment, so that patients with early swelling can be referred to lymphedema treatment specialists at a time when treatment is more effective.
Lymphedema: A primer on the identification and management of a chronic condition in oncologic treatment.	CA Cancer J Clin 2009;59:8-24.	Lawenda BD, Mondry TE, Johnstone PA.	2009	Generic	Review focuses on early identification and management of lymphedema along with pre-surgical assessment of risk. Supports BIS as reliable and accurate measure.
Addressing the Unmet Needs in Lymphedema Risk Management.	Lymphat Res Biol 2006;4:42-6.	Rockson SG.	2006	Generic	Addresses difficulties in lymphedema diagnosis and management suggesting that new diagnostics are needed for early subclinical detection.
Bioelectrical Impedance Analysis: Proven Utility in Lymphedema Risk Assessment and Therapeutic Monitoring.	Lymphat Res Biol 2006;4:51-6	Ward LC.	2006	Breast Ca	Supports BIS as a diagnostic modality with potential for earlier detection and feasible implementation into clinic.

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<b>Editorials</b>					
Is BIS ready for prime time as the gold standard measurement?	Journal of Lymphoedema 2009;4:52-6.	Ward L.	2009	Breast Ca	Editorial suggests that BIS should be considered new standard for lymphedema assessment due the sensitivity, specificity, and reproducibility of results.