impedimed

# The Future of Survivorship

April 29, 2017

impedimed

# Presenters

## Chirag Shah, MD

Associate Staff and Director of Clinical Research,

Department of Radiation Oncology

Cleveland Clinic, Cleveland, Ohio

***L-Dex Clinical Guidelines and Incorporation into Clinical Practice***

## David Kaufman, MD

Clinical Assistant Professor of Surgery

Hofstra-Northwell School of Medicine

Chief of Breast Surgery and Director of the Breast Surgery Program

St. Joseph Hospital, Bethpage, New York

***Experience with L-Dex in Routine Clinical Practice***

## Frank Vicini, MD

Clinical Professor, Radiation Oncology,

UCLA School of Medicine

Michigan Healthcare Professionals / 21st Century Oncology

Farmington Hills, Michigan

***Importance of Body Composition Analysis in Cancer Survivorship***

# L-Dex Clinical Guidelines and Incorporation Into Clinical Practice

Chirag Shah, MD
Associate Staff
Director of Clinical Research
Department of Radiation Oncology
Cleveland Clinic

# Disclosures

- Scientific Consultant- Impedimed Inc.

# Breast Cancer Related Lymphedema

- Increasing prevalence with improved breast cancer survivorship
- Rates vary widely
  - Locoregional treatment
  - Diagnostic techniques utilized
- Significant impact on QOL and function
- Focus on survivorship
  - Assess for risk factors to develop BCRL
  - Diagnose and treat BCRL
- Treatment
  - Minimally Invasive Sleeves
  - Complex Decongestive Physiotherapy
  - Lymph Node Transfer/Bypass/Liposuction

# Risk Factors

- Patient- BMI, Smoking
- Surgery- Mastectomy, ALND
- Radiation- Regional Nodal Irradiation
- Chemotherapy- Taxanes

# Risk Factors

Table 2. Incidence of lymphedema stratified by surgical procedure, axillary management, and RT

| Procedure | Risk of lymphedema (%) |
|---|---|
| Lumpectomy alone (9, 10) | 0–3 |
| Lumpectomy with SLN and breast RT (2, 6, 7, 14, 15, 18, 19) | 3–23 |
| Lumpectomy with ALND and breast RT (2, 6, 7, 11, 13, 14, 15, 16, 17) | 1–61 |
| Lumpectomy with regional nodal RT (2) | 9–65 |
| Mastectomy with SLN, no RT (2, 18, 19) | 3–23 |
| Mastectomy with ALND, no RT (2, 5, 17) | 30–47% |
| Mastectomy with regional nodal RT (2, 5) | 58–65 |
| ALND with axillary RT (12) | 32 |
| Radical mastectomy (5) | 58 |

*Abbreviations:* ALND = axillary lymph node dissection; SLN = sentinel lymph node; RT = radiation therapy.

# Diagnosis of BCRL

- Traditional Techniques
  - Circumference Measurements/Water Displacement
    - Variability in techniques
    - Low Sensitivity
    - Inter/Intraobserver variability
    - What is the Trigger to Treat?
- Need for high sensitivity, consistent technique with defined thresholds for treatment

# Diagnostic Modalities

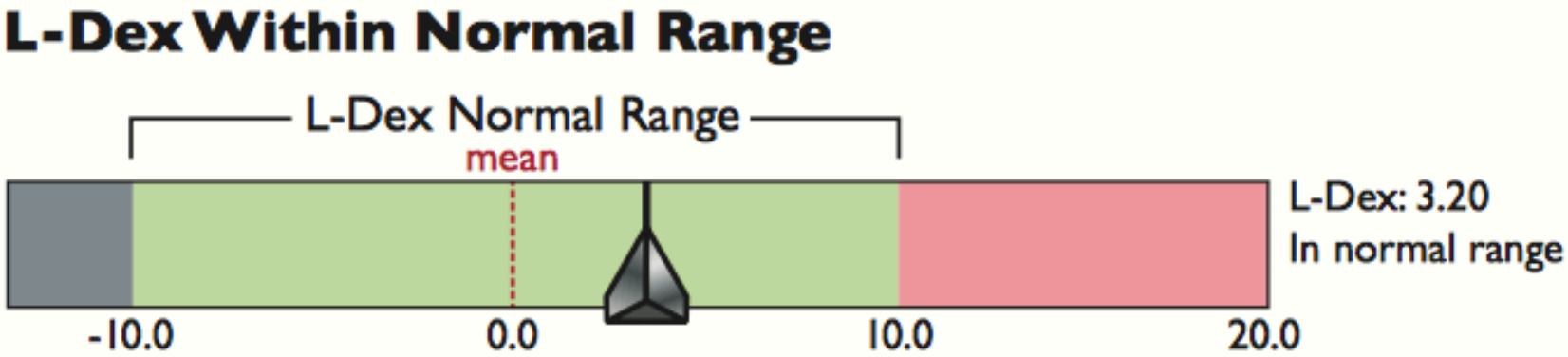
**Table 2. Comparison of Diagnostic Modalities for BCRL**

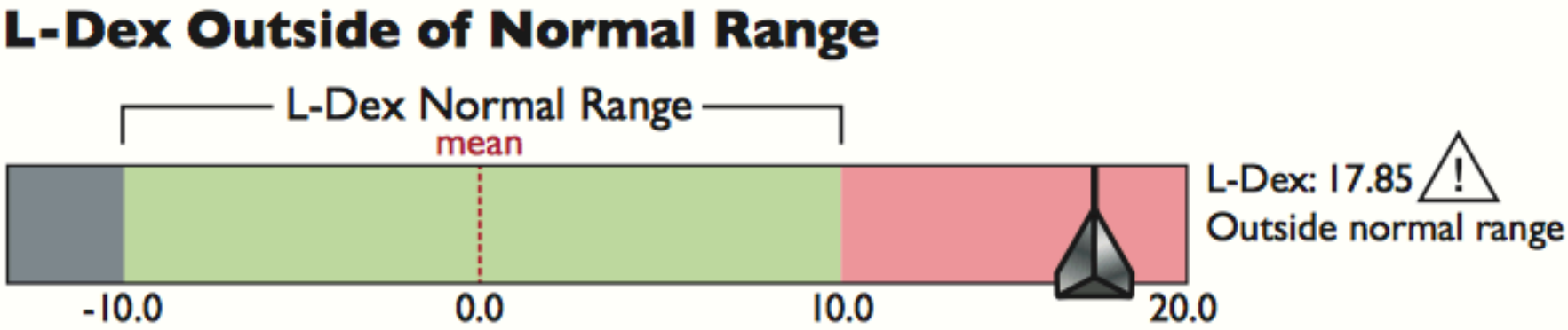
| | Pros | Cons |
|---|---|---|
| Circumference measurements | • Easy to perform<br>• Low cost<br>• Portable<br>• Used in multiple randomized trials | • Low sensitivity<br>• Inability to detect subclinical disease<br>• No consensus on standardized metrics to initiate therapy |
| Water displacement | • Easy to perform<br>• Used in previous studies | • Low sensitivity<br>• Inability to detect subclinical disease<br>• No consensus on standardized metrics to initiate therapy<br>• Cannot utilize in patients with infection |
| Patient survey | • Easy to perform<br>• Low cost | • Low sensitivity<br>• Inability to detect subclinical disease |
| Perometry | • Increased sensitivity | • High cost<br>• Space requirements<br>• Lack of long term data |
| Bioimpedance spectroscopy | • Highly sensitive<br>• Able to detect subclinical disease<br>• Standardized techniques<br>• Set cut offs to initiate treatment<br>• Portable<br>• FDA clearance | • Lack of long term data<br>• Cannot use on patients with implanted electronic devices (pacemaker, ICD)<br>• Cannot use on pregnant patients |

# Bioimpedance Spectroscopy

- Measures resistance of electrical (imperceptible) current flow through the body
- Current place through electrodes and change in voltage measured
- L-Dex score translates this into quantitative measure for physicians
  - Validated
  - Comparison of ratio of extracellular fluid differences between affected and non-affected arms and normal range
  - Ex. Impedance ratio = to healthy population translates to L-Dex score of 0
- Trigger:
  - L-Dex increase > 10 from pre-treatment baseline correlates with increase greater than 3 SD

# Bioimpedance Spectroscopy



# Bioimpedance Spectroscopy

**Table 3. Bioimpedance Spectroscopy Key Studies**

| | |
|---|---|
| Validation studies | |
| Berlit et al. (51) | Bioimpedance measured pre and postoperatively in cohort of 33 patients with breast cancer. Bioimpedance measures found to have good sensitivity and specificity as well as high negative predictive value |
| Ward et al. (52) | Healthy controls utilized to determine normal distribution, reference range, and threshold values |
| Ridner et al. (37) | Using single frequency bioimpedance, study found that impedance ratios similar for healthy controls, and breast cancer patients without BCRL; however, patients with BCRL had different impedance ratios than either group ($p < 0.001$) |
| Cornish et al. (33) | Prospective study utilizing multifrequency bioimpedance (MFBIA). Identified normal ratios in healthy controls. Among breast cancer patients, MFBIA identified BCRL up to 10 months earlier than clinical diagnosis; sensitivity/specificity 100%/98% |
| Diagnostic comparison | |
| Smoot et al. (45) | BIS yielded highest accuracy of diagnostic modalities employed with arm circumference (2 cm) having the lowest accuracy |
| Czerniec et al. (42) | In patients with upper limb edema, BIS had higher ratios than perometry, highlighting increased sensitivity |
| Hayes et al. (41) | Study of 287 women comparing BIS, circumference measurement, and self-reporting. 40–60% of cases identified by BIS not identified with self-report or circumference measurement |
| Ward (38) | Compared with tape measurement or water displacement, bioimpedance was more consistent with repeated measurements |
| Implementation/feasibility | |
| Ridner et al. (47) | Pilot study at Vanderbilt University of 50 patients; feasibility of self-care and bioimpedance with improved utilization of compression garments when patients utilized bioimpedance |
| Vicini et al. (40) | Study of 64 patients followed with bioimpedance in breast clinic. Bioimpedance measurements correlate with extent of locoregional treatment |

# Why Now?

- Growing Focus on Early Detection and Treatment of BCRL
- Stout et al
  - 196 patients prospectively followed
  - 43 with early BCRL treated with conservative compression garments
  - Reduced arm volumes, need for further treatment
- Soran et al
  - 186 patients undergoing ALND- followed prospectively with BIS
  - Subclinical BCRL- short term PT, compression garment, eduction
  - Control group- upfront L-Dex measurement, only circumference after
  - Progression to clinical BCRL 4.4% L-Dex vs. 36.4% control
- Need sensitive diagnostic technique to allow for early detection and treatment
  - Bioimpedance Spectroscopy

# Early Detection of BCRL

**Table 1. Trials Evaluating the Role of Early Detection & Management of BCRL**

| Institution | Number of patients | Early intervention technique | Results |
|---|---|---|---|
| Prospective randomized | | | |
| Alcala de Heneres University (14) | 120 | Manual lymphatic drainage, massage, exercise, education versus education | 1 year: BCRL 7% early intervention versus 25% education alone ($p = 0.01$) |
| University of Queensland (15) | 65 | Physiotherapy versus surveillance | 2 years: BCRL 11% physiotherapy versus 30% surveillance |
| Prospective | | | |
| National Naval Medical Center (16) | 196 | Compression garment | Average 4-week utilization, 48 mL decrease. Volume decrease maintained with follow-up |
| University of Pittsburgh Medical Center (12) | 186 | Physical therapy, compression garment, education | Compared with control, early intervention reduced the incidence of clinically diagnosed lymphedema (36.4% versus 4.4%) |
| Retrospective | | | |
| University of New Mexico (17) | 69 | – | Patients who started with lower limb volumes (<250 mL) had improved response to intervention compared with those with higher volumes (250–500 mL): 78% reduction versus 56% reduction |
| Lund University (18) | 292 | – | BCRL can be kept at low volumes with early detection and intervention for 10 years. Smaller volume at diagnosis correlated with lower risk of developing significant BCRL in the future |

# Current Guidelines

National Comprehensive Cancer Network®

**NCCN Guidelines Version 2.2017**
**Invasive Breast Cancer**

**SURVEILLANCE/FOLLOW-UP**

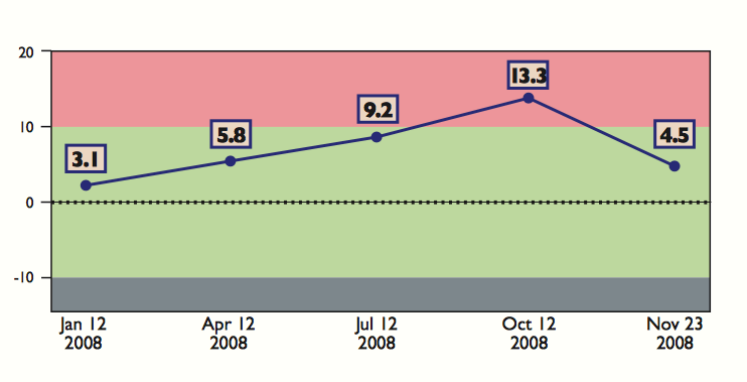
- History and physical exam 1–4 times per year as clinically appropriate for 5 y, then annually
- Periodic screening for changes in family history and referral to genetic counseling as indicated, see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian
- Educate, monitor, and refer for lymphedema management
- Mammography every 12 mo[oo]
- Routine imaging of reconstructed breast is not indicated
- In the absence of clinical signs and symptoms suggestive of recurrent disease, there is no indication for laboratory or imaging studies for metastases screening
- Women on tamoxifen: annual gynecologic assessment every 12 mo if uterus present
- Women on an aromatase inhibitor or who experience ovarian failure secondary to treatment should have monitoring of bone health with a bone mineral density determination at baseline and periodically thereafter[pp]
- Assess and encourage adherence to adjuvant endocrine therapy
- Evidence suggests that active lifestyle, healthy diet, limited alcohol intake, and achieving and maintaining an ideal body weight (20–25 BMI) may lead to optimal breast cancer outcomes
- See NCCN Guidelines for Survivorship

# Who Should Undergo Surveillance?

- Any patient?
  - Cost and use of resources
- High Risk Patients
  - Mastectomy
  - ALND
  - > 6 LN sampled
  - Regional Nodal Irradiation
  - Taxane based chemotherapy
  - Elevated BMI

# L-Dex Clinical Guidelines

- Shah et al- Breast Journal 2016
- Eligibility
  - Not pregnant
  - No pacemaker/implanted device/metal implant in arm, shoulder



# Technique

3 Have patient remove shoes, socks, watches, bracelets, necklaces, and anklets.

4 Have patient lay down on a nonmetal bed.

5 Use an alcohol wipe to clean the back of both of wrists next to the wrist joint, both of hands in the center, and the top of the right foot and ankle.

6 Line up the green line located on the electrode between the two ankle bones on top of the right foot.

7 Place electrodes on the back of each hand, lining up the green line on the pad between the two wrist bones and then placing the rest of the pad down the hand toward the second knuckle.

8 Ensure electrodes have completely adhered to the skin.

9 Attach clips to electrodes as directed and begin right arm measurement.

10 Repeat process above for left arm.

Note: Measurement should be taken after patient has been supine for 3 minutes but no more than 10 minutes.

# Current L-Dex Guidelines

- Protocol
  - Begin prior to locoregional/neoadjuvant therapy to establish baseline
  - Repeat measurements q3 months X 3 years (highest incidence)
  - Then yearly
- Detection
  - A change greater than 10 can be used to initiate treatment

# Feasibility

- Average time < 5 minutes including preparation

## Bioelectrical Impedance for Detecting and Monitoring Patients for the Development of Upper Limb Lymphedema in the Clinic

Frank Vicini,[1,2] Chirag Shah,[2] Maureen Lyden,[3] Pat Whitworth[4]

**Abstract**

**Limited data are available on new diagnostic modalities in breast cancer–related lymphedema. Analysis of the implementation of bioimpedance spectroscopy to detect breast cancer–related lymphedema in the community oncology setting demonstrated its feasibility and simplicity. Further, in 64 patients, analysis within 90 days of surgery demonstrated that bioelectrical impedance had the ability to detect differences based on surgical and axillary procedure, which potentially allows for subclinical diagnosis.**

**Background:** Single-frequency bioelectrical impedance (BI) has been used to measure extracellular fluid in the upper limbs. The purpose of the study was to evaluate BI's ability to detect and monitor upper limb changes in based upon the extent of various treatments and to assess its practicality. **Methods:** Patients with newly diagnosed breast cancer were evaluated at baseline and after procedures that could potentially affect fluid accumulation in the arm and signal the possible development of early lymphedema. The magnitude of the change in lymphedema index ratios (LIR) from these procedures was evaluated to determine the sensitivity of BI. **Results:** A total of 64 patients were evaluated. Although no difference in LIRs was noted by the extent of surgical procedure (lumpectomy 2.1 vs. mastectomy 1.1; $P = .49$), a trend was noted for increased LIRs with more aggressive axillary staging when sentinel lymph node was compared with axillary lymph node dissection (1.3 vs. 3.4; $P = .08$). A trend for an increased LIR with more aggressive local therapy also was noted when using a cutoff of less than 4 lymph nodes sampled compared with 4 or more nodes sampled (1.2 vs. 2.6; $P = .09$). **Conclusions:** In this limited analysis, L-Dex readings paralleled the extent of surgical interventions and suggest that they can be used to monitor patients for the early onset of edema. Further studies are needed to help validate the extent, degree, and chronologic time frame of these changes to help define recommendations for closer monitoring of patients and possible early intervention.

*Clinical Breast Cancer,* Vol. 12, No. 2, 133-7 
**Keywords:** Adverse effects, Bioimpedance, Community clinical oncology, Sensitivity, Subclinical diagnosis

# Conclusions

- Breast cancer related lymphedema has the ability to significantly impact quality of life
- High risk patients- Mastectomy, ALND, RNI, Chemotherapy, Elevated BMI
- Increasing data supports early detection and treatment to reduce chronic BCRL
  - Need sensitive diagnostic technique!
- Clinical guidelines with L-Dex exist
  - Defined trigger to initiate therapy
- Data demonstrating feasibility, efficacy of incorporating into clinics, survivorship programs

# Thank you

# Bio-Impedance Spectroscopy (BIS) Early Detection and Intervention for Breast Cancer-Related Lymphedema

David I. Kaufman, M.D., F.A.C.S

Chief of Breast Surgery St. Joseph Hospital
Director of Breast Care Specialists
Assistant Professor of Surgery
Hofstra Northwell School of Medicine

dkat727@aol.com
516-639-4221

# Prevalence and Incidence of Lymphedema

- 3 - 5 million patients in the USA suffer from lymphedema
- After standard lymph node dissection -15-35% of patients++
- 6-8% after sent node biopsy-increased with # of nodes bx'd
- Higher if:
  - Regional nodal irradiation
  - Heart disease
  - High BMI
  - Taxane chemotherapy??

# What is Breast Cancer-Related Lymphedema?

- Lymphatic pathways become disrupted due to loco-regional therapy (surgery or radiotherapy) and over time, the flow of lymph can overwhelm the remaining pathways, resulting in a backup of fluid into the body's tissues

## Stage 0 Lymphedema
# (NIH “Grade 1, acute or subclinical”)


- No apparent swelling
- May report vague “heaviness”
- Slower flow on Lymphoscintigraphy
- Detectable with Perometer or BIS (L-Dex)

Images provided for use by Dr Charles McGarvey and Guenter Klose

## Stage 1 Lymphedema
# (NIH “Grade 2, mild-acute”)


- Mild swelling
- Reversible with elevation of the arm
- Protein-rich extracellular fluid
- Detectable with all techniques

Images provided for use by Dr Charles McGarvey and Guenter Klose

## Stage 2 Lymphedema
# (NIH “Grade 3, moderate-chronic/clinical”)


- Mild to moderate swelling
- Minimal or no decrease with elevation
- Expanded extracellular fluid compartment
- Fibrosis: lifelong decongestive therapy (too late for prevention)

Images provided for use by Dr Charles McGarvey and Guenter Klose

## Stage 3 Lymphedema
# (NIH “Grade 4, severe”)


- Severe swelling
- No change with elevation
- Fibrosis and fat have replaced most of the fluid
- Little response to CDT (complex decongestive physiotherapy)

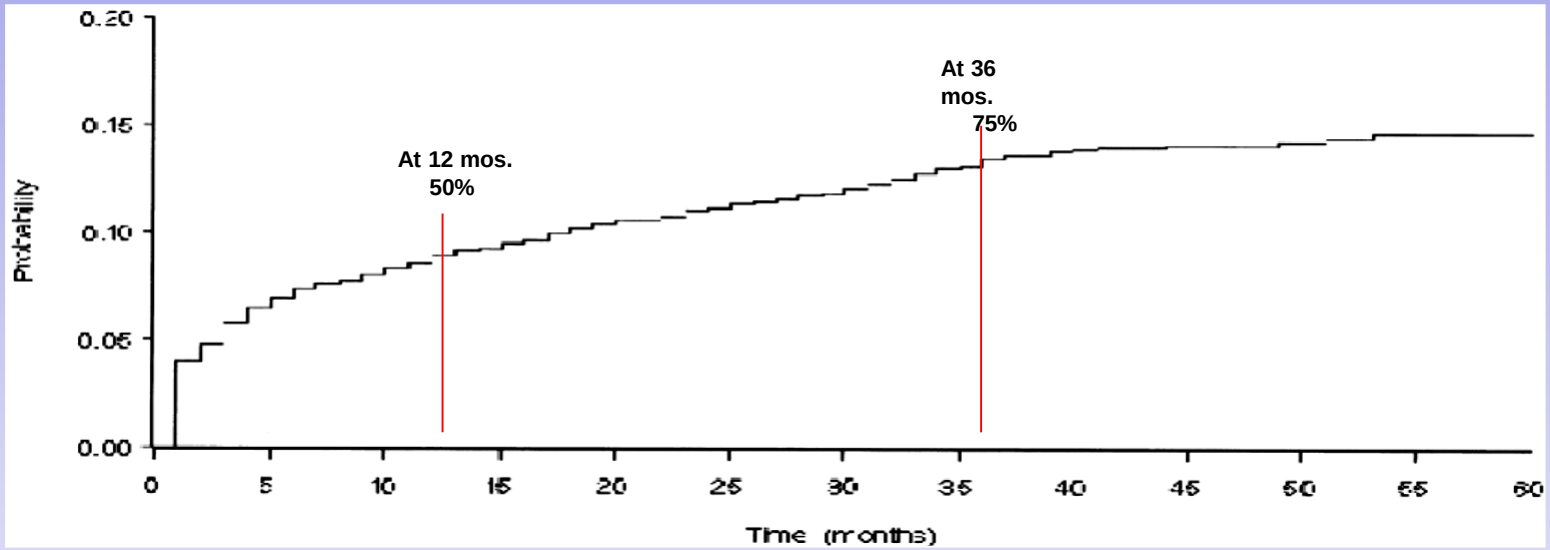
Images provided for use by Dr Charles McGarvey and Guenter Klose

# Incidence Depends on Cancer Treatment & Type

| Type of Cancer / Treatment | Pooled Lymph% |
|---|---|
| SLNB for Breast Cancer | 6.30% |
| ALND for Breast Cancer | 22.30% |
| SLNB for Melanoma | 4.10% |
| ALND for Melanoma | 3% |
| Inguinofemoral LND | 18% |
| Vulvar Cancer | 30% |
| Miscellaneous | 27% |
| SLNB for GYN Cancer | 9% |
| Head & Neck | 21% |
| Penile Cancer | 21% |
| Bladder Cancer | 16% |
| Prostate | 4% |
| **Radiation** | **%** |
| SLNB + Whole Breast Irradiation | 14.50% |
| ALND + Whole Breast Irradiation | 31.50% |
| SLNB + Whole Breast Irradiation+ Regional Lymph Node Irradiation | 41.40% |
| Genitourinary | 16% |
| Gynecologic | 34% |
| Melanoma | 50% |

Shaitelman, S. F., Cromwell, K. D., Rasmussen, J. C., Stout, N. L., Armer, J. M., Lasinski, B. B. and Cormier, J. N. (2015), Recent progress in the treatment and prevention of cancer-related lymphedema. CA: A Cancer Journal for Clinicians, 65: 55–81. doi: 10.3322/caac.21253

# When Do Patients Develop Lymphedema?




Herd-Smith, A., et al., *Prognostic factors for lymphedema after primary treatment of breast carcinoma.* Cancer, 2001. 92(7): p. 1783-7

# National Comprehensive Cancer Network® (NCCN®)

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are consistent with regards to the necessity **to educate patients about lymphedema and monitor for the early development of lymphedema**.

*NCCN Guidelines® for Breast Cancer, Version 2.2015*[1]
Under Surveillance/Follow-up, page BINV-16, the guidelines state:

- "History and physical exam 1-4 times per year as clinically appropriate for 5 y, then annually"
- "Educate, monitor, and refer for lymphedema management"

Page BINV-16 also states "See NCCN Guidelines for Survivorship"

*NCCN Guidelines for Survivorship, Version 1.2015*[2]
Under Physical Activity, page SPA-A, the guidelines state:
"Lymphedema:

- Undergo baseline and periodic evaluation for development or exacerbation of lymphedema"

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.2.2015. ©National Comprehensive Cancer Network, Inc 2014. All rights reserved. Accessed April 15, 2015. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Survivorship V.1.2015. ©National Comprehensive Cancer Network, Inc 2014. All rights reserved. Accessed April 15, 2015. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

# National Lymphedema Network (NLN) Position Statements

NLN Position Statement – Topic: Screening and Measurement for Early Detection of Breast Cancer Related Lymphedema

- Breast cancer treatment places individuals at life-long risk for the development of lymphedema. Early detection of lymphedema allows for early intervention that can prevent or slow progression of lymphedema to a chronic, harder-to-treat stage.
- Objective measurement: A pre-operative baseline measurement of arms or at least a post-operative should be a standard component of breast cancer care, which can be used to compare all subsequent measures throughout recovery and survivorship. Surgeons, medical oncologists, and Advanced Practice Nurses who treat patients with breast cancer should work collaboratively to establish follow-up care that includes measurements at each visit.

NLN – Lymphedema Screening and Treatment Recommendations

- To reduce the occurrence of false negative or false positive results, ideally these methods have little room for user error and therefore, bioelectrical spectroscopy (BIS) or infrared perometry are highly desired methods of alternative measurements.

# 2014 NAPBC Standards

## Standard 2.15 Support and Rehabilitation

Lymphedema management and risk reduction practices

Refers to NLN Screening and Measurement for Early Detection of Breast Cancer Related Lymphedema

- Pre-operative baseline measurement of arms should be a standard component of breast cancer care
- Each follow-up visit should include arm measurements using a standard reproducible, consistent method to enable comparison

## Standard 2.20 Breast Cancer Survivorship Care

NAPBC now includes a Survivorship Care requirement for accreditation.

Compliance includes:

- A comprehensive breast cancer survivorship care process, including a survivorship care plan with accompanying treatment summary is in place …
- A Follow-up Care section which may include, but is not limited to, information related to:
  - Referrals/resources as necessary to support the patient in achieving these lifestyle behavior changes successfully, i.e., rehabilitation for lymphedema, smoking cessation, weight management, or others

# NIH study: Benefit of early assessment


- 5 year prospective NIH study[1]
- Conducted at National Naval Medical Center
- NIH and Navy IRB oversight
- Utilized a standardized metric for assessment of total arm volume

- 196 breast cancer patients all with a pre-operative baseline
- Evaluated at 1, 3, 6, 9,12 and 18 months
- 43 (22%) were identified with sub-clinical lymphedema, average time to onset 6.9 months
- Intervention with off-the-shelf compression sleeve (4.4 weeks average)
- All 43 reverted statistically back to a pre-surgical baseline

1. Stout Gergich, N.L., et al., *Preoperative assessment enables the early diagnosis and successful treatment of lymphedema.* Cancer, 2008. 112(12): p. 2809-19

# Efficacy of subclinical lymphedema detection (2014)

Magee-Womens Hospital of UPMC

UPMC LIFE CHANGING MEDICINE

- 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.
  - N=180
  - Measurement interval: pre-operative, 3-6 months post-surgery, then annually for 5 years.
  - Control group (44) had a preoperative baseline L-Dex measurement, but had only clinical follow-ups with circumferential arm measurements. 36.4% (16/44) developed clinical lymphedema.
  - Non-control group patients, 33% were diagnosed with subclinical LE (45/136) and through early intervention received short-term physical therapy and compression garments.
  - After an average 21 month follow-up, only 4.4% (2/45) progressed to clinical lymphedema.

**Periodic monitoring of women at high risk for LE with BIS allows early detection and timely intervention for LE, which reduces the incidence of clinical LE from 36.4% to 4.4%. This may have implications for quality of life and health care costs.**

Soran, A., et al., *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, 2014. 12(4): p. 289-94

# Traditional Techniques for Lymphedema Detection

## Water Displacement

## Circumference Measurements

**>2 cm increase in circumference <u>or</u> 200 ml (≈ 5% volume Δ) by truncated cone method (superior)**

# Contemporary Lymphedema Assessment Techniques

Perometer (optical scan)

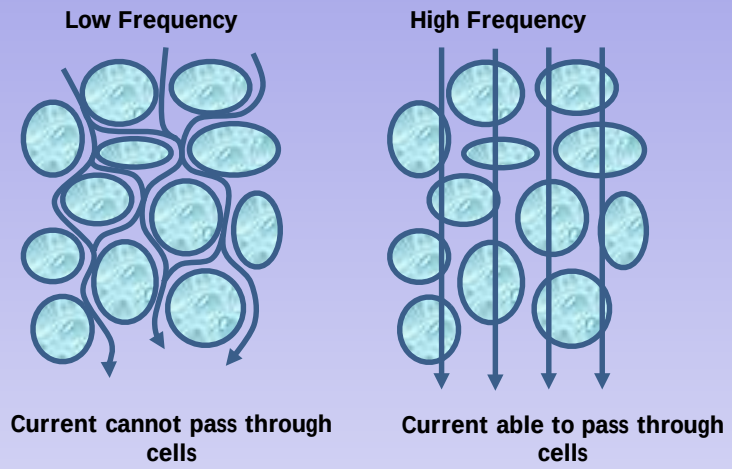
100 ml ≈ 3 % volume Δ

Bioimpedance Spectroscopy (BIS)

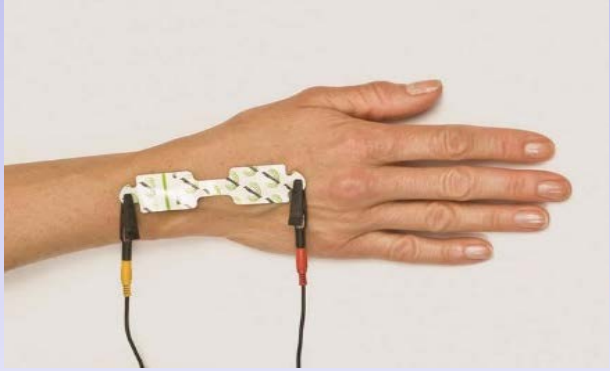

10 L-Dex® units increase from baseline

# Proactive Measurement Tool: Bioimpedance Spectroscopy (BIS)

- BIS technology directly measures the extracellular fluid
- Passes a low-level signal through the body's fluids
- Measures body's impedance to the flow of the current
- Harmless, painless, rapid
- Low frequency only travels through extracellular space
- Electrode placement determines field of measure



# What is L-Dex?



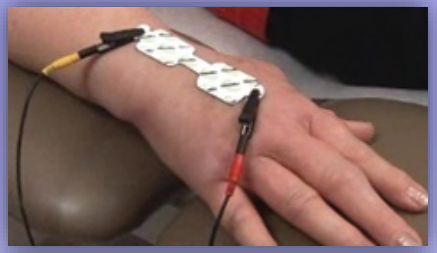
- FDA-cleared Class II medical device
- Sensitive – can detect subclinical lymphedema before visible swelling {clinical/chronic}
- Specific – detects only extracellular fluid
- Reproducible
- Simple to perform
- Rapid – minutes
- Handheld and portable
- Non-invasive
- BIS detects lymphedema up to 200 days prior to volume measurements[1].

Cornish, B.H., et al., *Early diagnosis of lymphedema using multiple frequency bioimpedance.* Lymphology, 2001. 34(1): p. 2-11

# Taking a Measurement with L-Dex™ U400

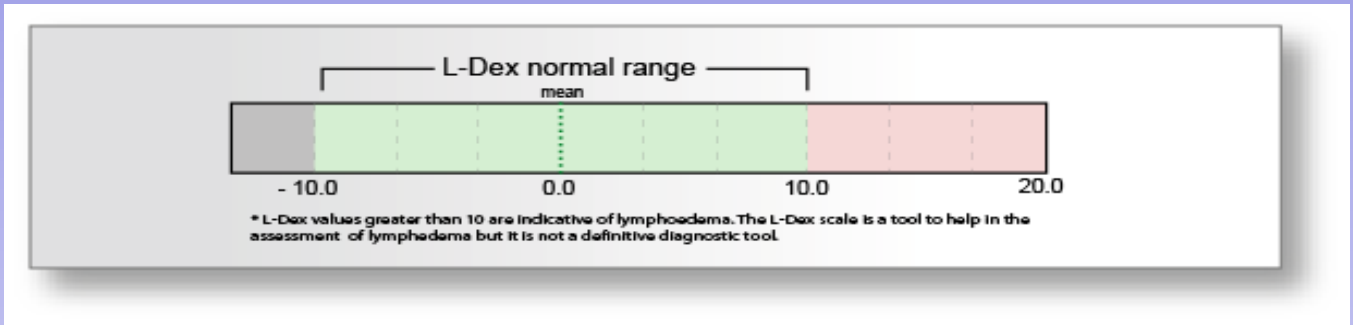
Patient assumes a supine position

- Sites for electrode / lead placement are cleaned then placed
- Following prompts, measure ECF in each limb
- L-Dex score is generated

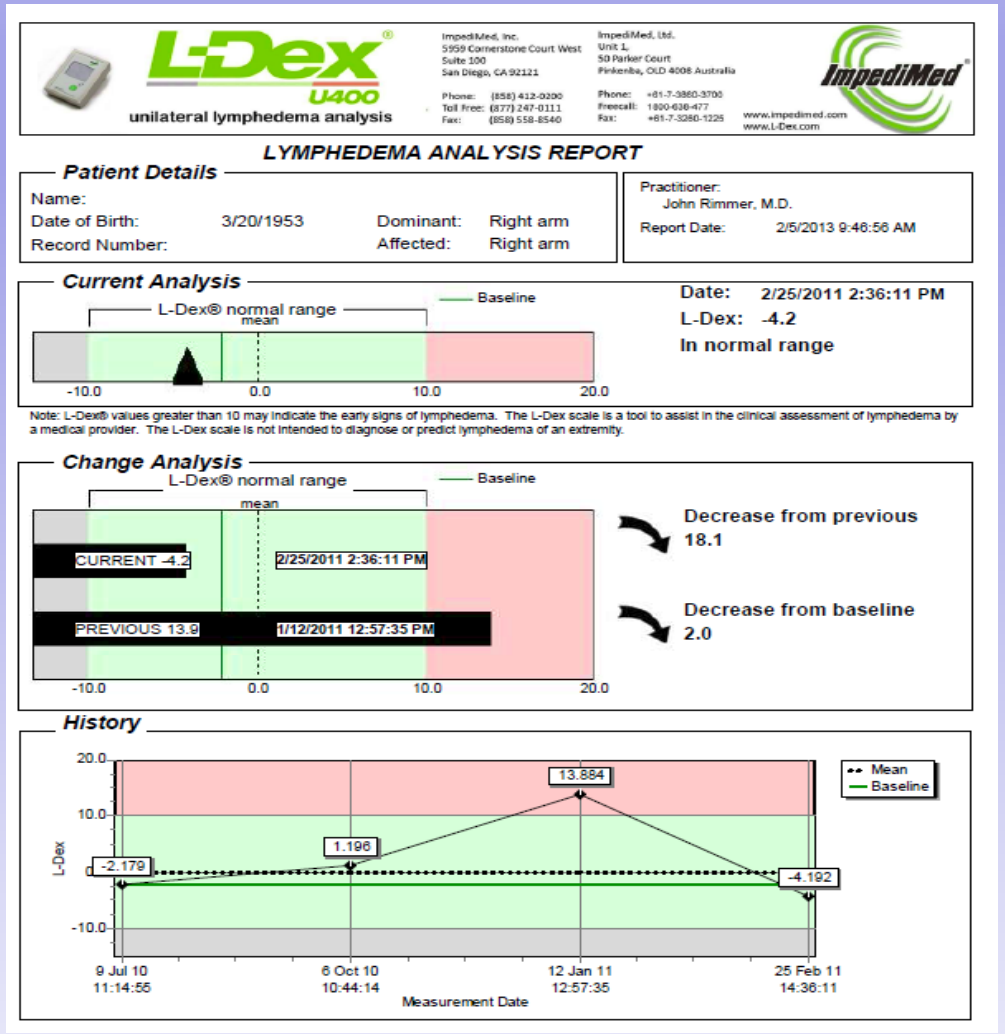


Contra-indications : Pregnancy & Pacemaker

# Understanding the L-Dex scale




- Normal range for L-Dex was established from bioimpedance data gathered from a cross **population study of healthy women**. **The mean (average)** L-Dex value of healthy women without lymphedema, regardless of arm dominance**, is defined as 0.0** within this normal range.
- **L-Dex values of +10 and -10 represent three standard deviations (3 SD) from the mean in a population of women without lymphedema.**



L-Dex® U400
unilateral lymphedema analysis

ImpediMed, Inc.
5959 Cornerstone Court West
Suite 100
San Diego, CA 92121
Phone: (858) 412-0200
Toll Free: (877) 247-0111
Fax: (858) 558-8540

ImpediMed, Ltd.
Unit 1,
50 Parker Court
Pinkenba, QLD 4008 Australia
Phone: +61-7-3860-3700
Freecall: 1800-636-477
Fax: +61-7-3260-1225

www.impedimed.com
www.L-Dex.com

ImpediMed®

## LYMPHEDEMA ANALYSIS REPORT

### Patient Details

Name:
Date of Birth: 3/20/1953
Record Number:
Dominant: Right arm
Affected: Right arm

Practitioner:
John Rimmer, M.D.
Report Date: 2/5/2013 9:46:56 AM

### Current Analysis

L-Dex® normal range
mean
Baseline
-10.0 0.0 10.0 20.0

Date: 2/25/2011 2:36:11 PM
L-Dex: -4.2
In normal range

Note: L-Dex® values greater than 10 may indicate the early signs of lymphedema. The L-Dex scale is a tool to assist in the clinical assessment of lymphedema by a medical provider. The L-Dex scale is not intended to diagnose or predict lymphedema of an extremity.

### Change Analysis

L-Dex® normal range
mean
Baseline
CURRENT -4.2
2/25/2011 2:36:11 PM
PREVIOUS 13.9
1/12/2011 12:57:35 PM
-10.0 0.0 10.0 20.0

Decrease from previous
18.1

Decrease from baseline
2.0

### History

L-Dex
20.0
10.0
0
-10.0
13.884
1.196
-2.179
-4.192
Mean
Baseline
9 Jul 10 11:14:55
6 Oct 10 10:44:14
12 Jan 11 12:57:35
25 Feb 11 14:36:11
Measurement Date

# Prospective Surveillance for BCRL
## My Clinical Experience

### 2010 to Present

# Surveillance Protocol

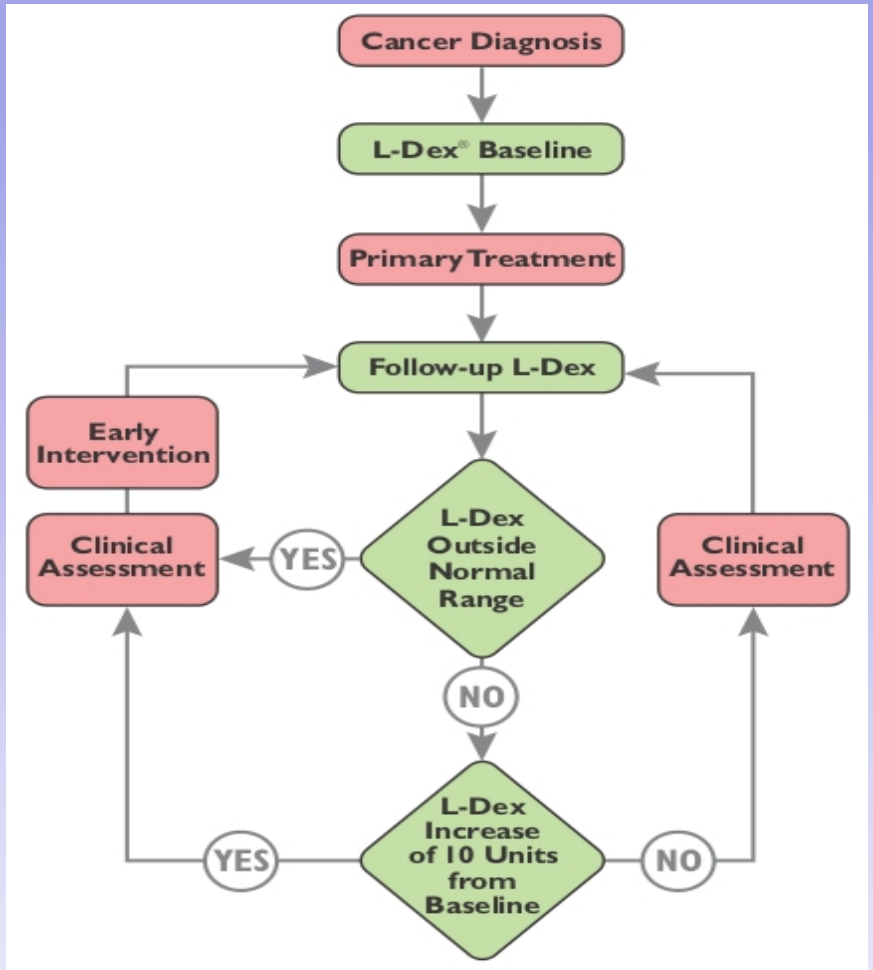
- All Diagnosed BC Patients with Planned Nodal Dissection/Sentinel Node Biopsy

- Assessment Schedule:
  - Pre-operative baseline and 6 weeks post-op
  - Years 1-3: Every 3 months
  - Years 4-5: Every 6 months
  - Year 6+: Annually

- If BIS score increments 10 units above baseline:
  - Referral to PT to Include OTC Sleeve for 4 Weeks

- Re-Assess with L-Dex for resolution
  - If yes, continue surveillance
  - If no and symptomatic, continue PT oversight
  - If no and asymptomatic, continue surveillance (and sleeve until resolution)

# Surveillance Protocol




Return to Index

# ASBrS 2017 Las Vegas - Data Presentation

- Retrospective analysis of 264 patients prospectively surveilled for the development of breast cancer-related lymphedema (BCRL) using BIS-2010 to present
- All patients had baseline assessment and a minimum of 2 post-op follow up assessments
- 28 patients (10.6%) had an elevated L-Dex score (10 points or more from baseline) at some point during follow-up/surveillance
- All 28 underwent treatment with a compression sleeve for 4 weeks

## ASBrS 2017 Las Vegas - Data Presentation

- At last follow-up- 4 patients (1.5% of total cohort) had persistently elevated L-Dex scores, yet remained asymptomatic
- 0% of patients progressed to complex decongestive P-therapy (CDP)

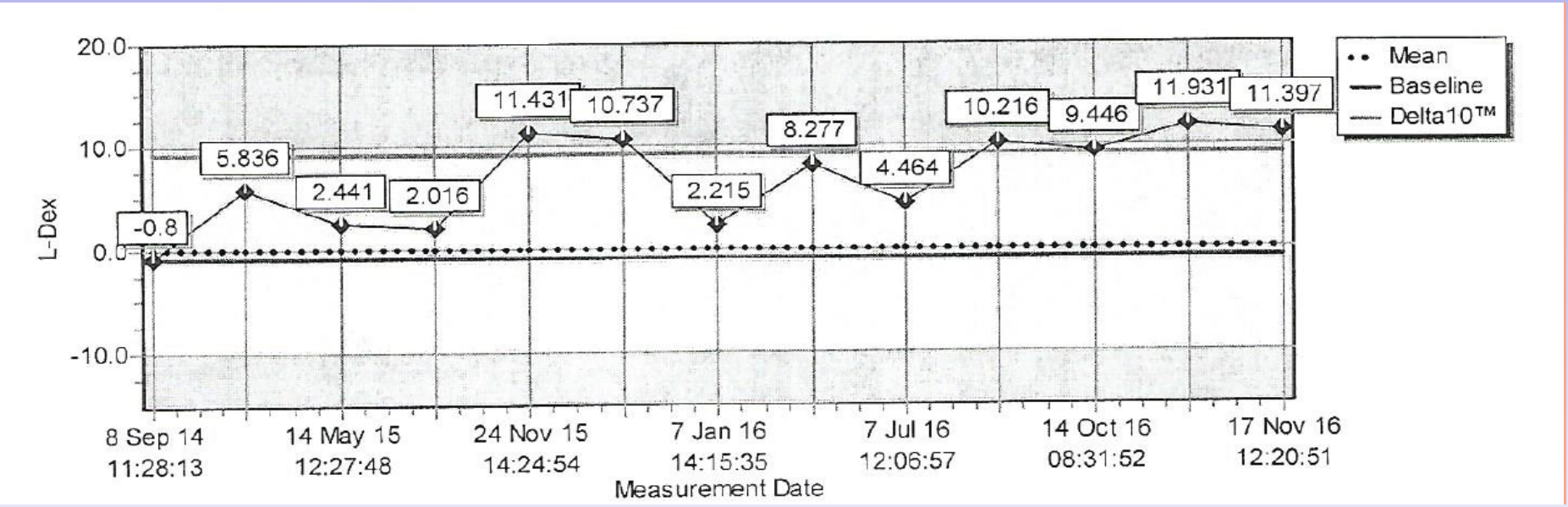
**Conclusion:**

**Prospective surveillance using BIS with early intervention in the subclinical/acute phase of BCRL led to low rates of persistently elevated L-Dex scores and no cases of clinically symptomatic BCRL/chronic/irreversible phase**

# Case Studies

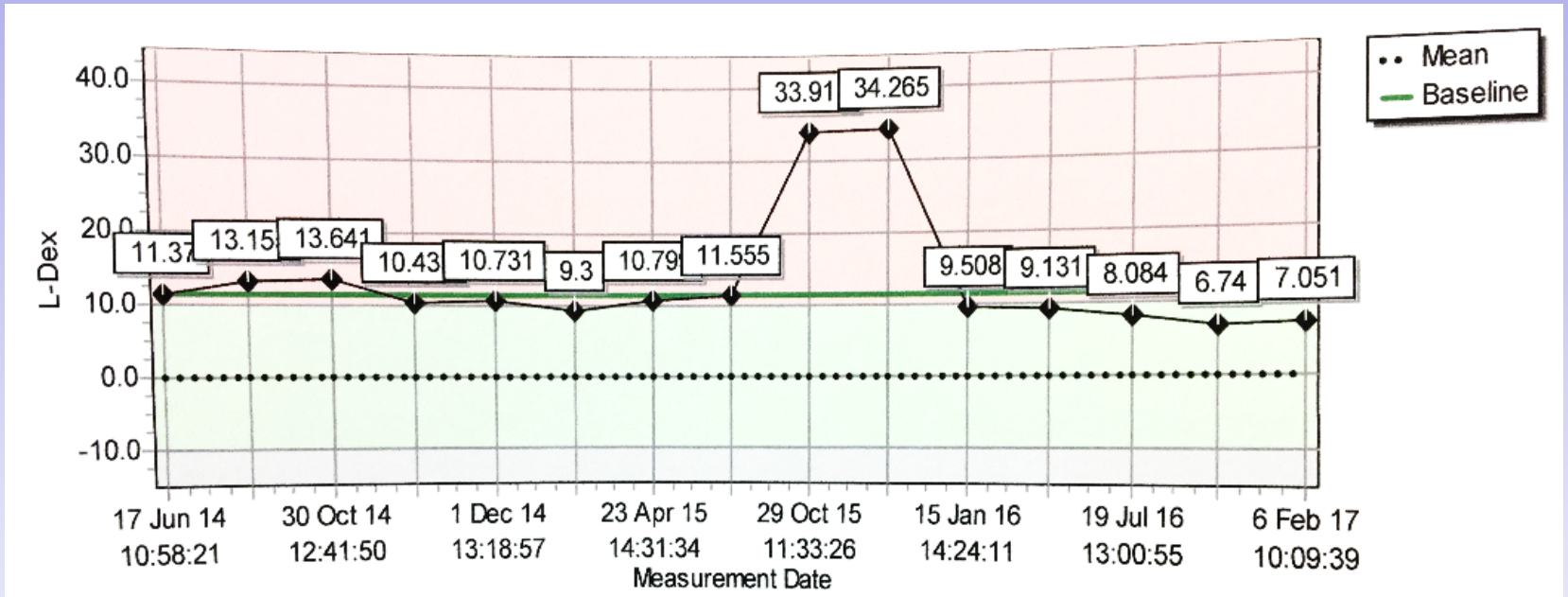
## 73 y/o w/f - Left Lumpectomy, ALND, WBI, RNI (Axilla), Hormonal Tx, 11/2014

- L-Dex Score Elevated 10+ Pts, 1 year after surgery
- Referred to PT for oversight
- L-Dex Score remains stable and patient remains asymptomatic



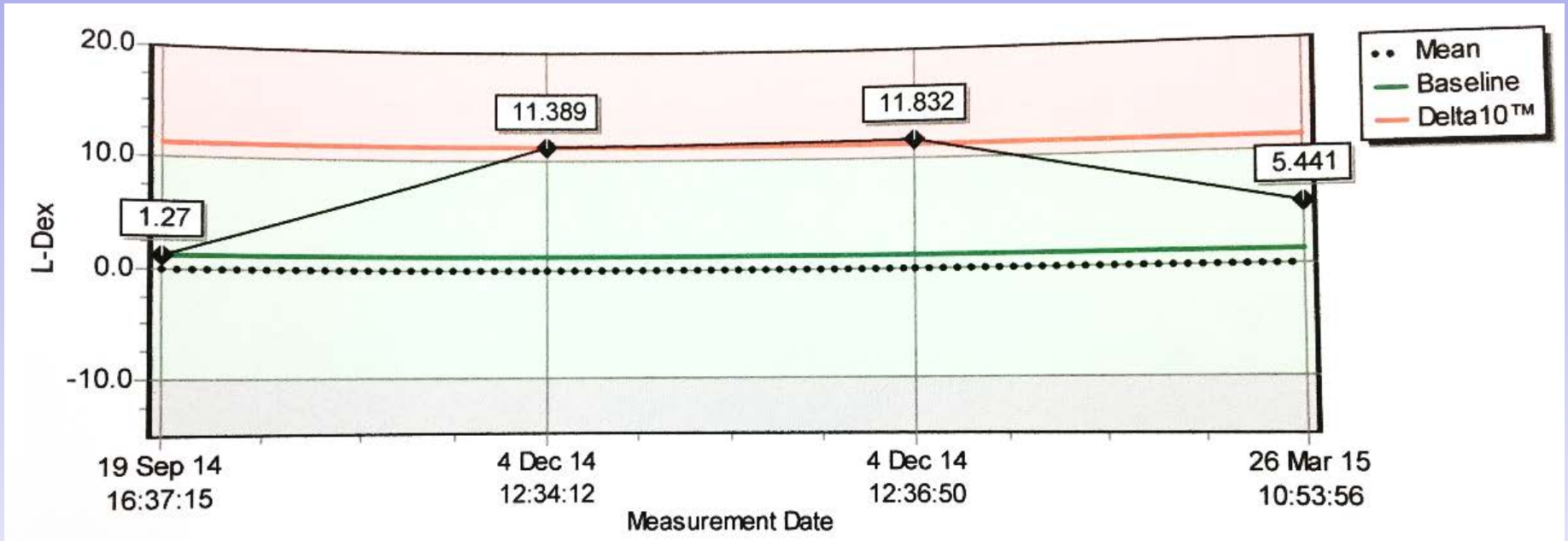
## 70 y/o b/f–LAC-- Neo Adjuvant Chemo-Taxane + Mastectomy + ALND 7/2014 + CWI + Regional Nodal Irradiation (Axilla) + Endocrine Therapy

Early Post Op—
SX-- P/T referral – Compression Sleeve and physical therapy prescribed
Pt had difficulty with sleeve comfort resulting in decrease use and elevation of the L-Dex score
P/T instructed pt. in properly placing the sleeve for comfort and use resumed. Score declined and no sign of clinical lymphedema to date



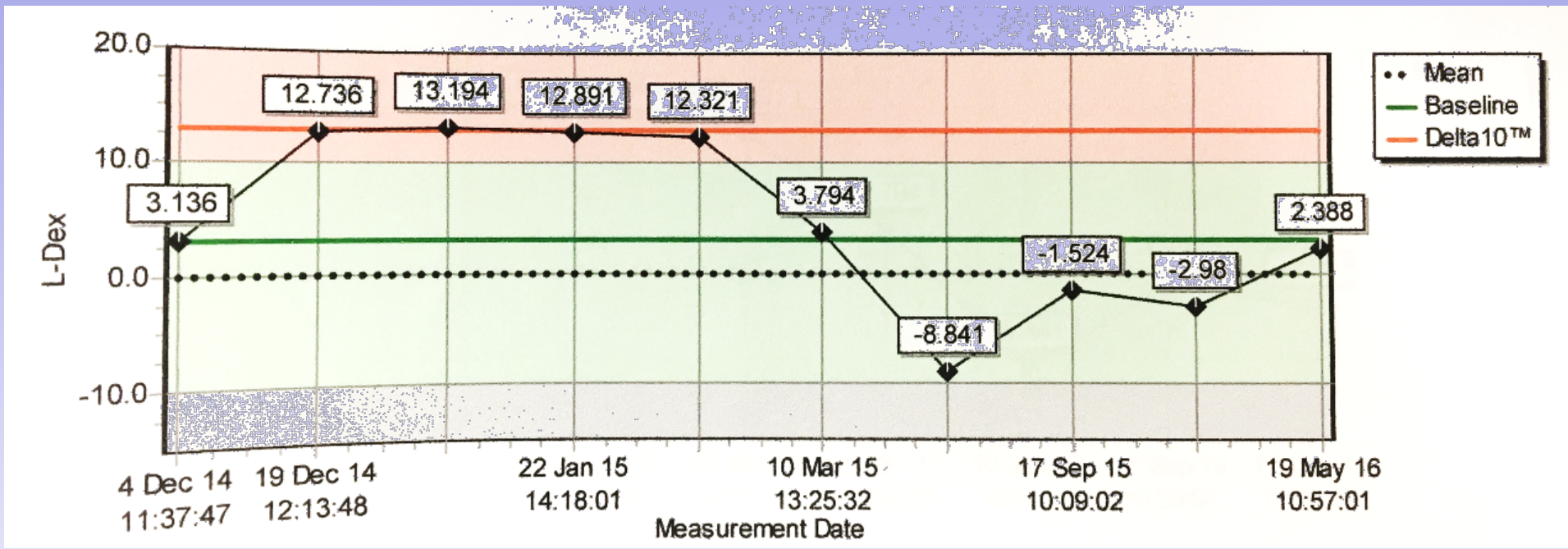
## 79 y/o w/f - Left Lump + SLNB + Hormonal Tx - Oct 2014

**L-Dex score elevated 10+, went into OTC sleeve for 4 weeks, score reverted, patients remains asymptomatic, continued surveillance**



**74 y/o w/f - RT Lumpectomy, SLNB, WBI, Hormonal Tx - Dec 2014**

**L-Dex score elevated 10+, went into OTC sleeve for 4 weeks, score returned to normal range, patients remains asymptomatic, no sign clinical LE……. surveillance**



# Conclusion

- Lymphedema is not just a swelling of the limb
- Once established as a chronic condition there are significant physical, quality of life, costly and psychological complications
- BIS represents the best opportunity for early detection of lymphedema, {objective}
- Early detection has been shown to reduce the risk of progression to a chronic condition leading to a reduction of costs to the patient and the healthcare system, less disability
- BIS allows compliance with NCCN and NIH guidelines using a standardized, objective measuring protocol


ST. JOSEPH
EMERGENCY
AMBULATORY

# Thank you

dkat727@aol.com
516-639-4221

# *Importance of Body Composition Analysis in Cancer Survivorship*

**Frank Vicini, MD, FACR**
**Clinical Professor, Radiation Oncology**
**UCLA School of Medicine**
**Michigan Healthcare Professionals/21st Century Oncology**
**Farmington Hills, Michigan**
**April 29, 2017**

# *Bioimpedance Spectroscopy (BIS)*

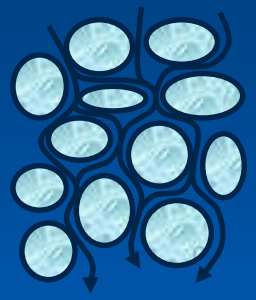
- Can BIS technology be used to optimize treatment outcomes, reduce cancer treatment related toxicities and improve QOL by impacting patient health (Cancer Survivorship)?

# Bioimpedance Spectroscopy - BIS

**A rapid, non-invasive system that provides highly accurate data**

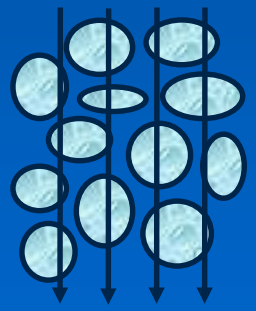
**Simple & Sophisticated Method for Measuring Fluid & Tissue Composition**

**Low Frequency**



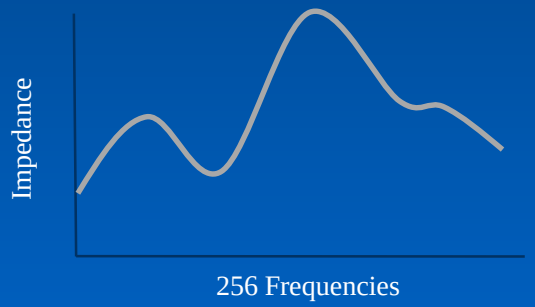
**Current passes around cells**

**High Frequency**

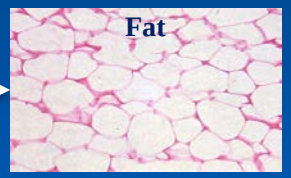


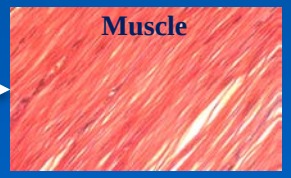
**Current passes through cells**

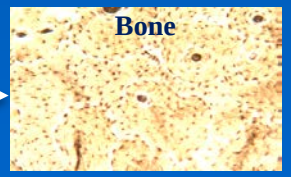
**Unique Spectra**







# BIS Science

- By passing a low level electrical current through the body at many frequencies, BIS is able to differentiate fluid and tissue volumes
- BIS is an accurate and noninvasive way of measuring fluid and tissue composition of the body
- BIS correlates very closely with more invasive, technical and costly technology


1. Thomson, R., et al., *Good agreement between bioelectrical impedance and dual-energy X-ray absorptiometry for estimating changes in body composition during weight loss in overweight young women.* Clin Nutr, 2007.
2. Moon, J.R., et al., *Total body water estimations in healthy men and women using bioimpedance spectroscopy: a deuterium oxide comparison.* Nutr Metab (Lond), 2008. **5**(1): p. 7.

# What is Survivorship?

- An individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life.
- This includes potential impact on health, physical and mental states
- As cure rates increase, cancer survivorship takes on greater significance in our patients

NCCN Survivorship guidelines

# What affects Survivorship?

- Key Components:
  - I. Weight management
  - II. Chemotoxicity
  - III. Sarcopenia
  - IV. Bone density

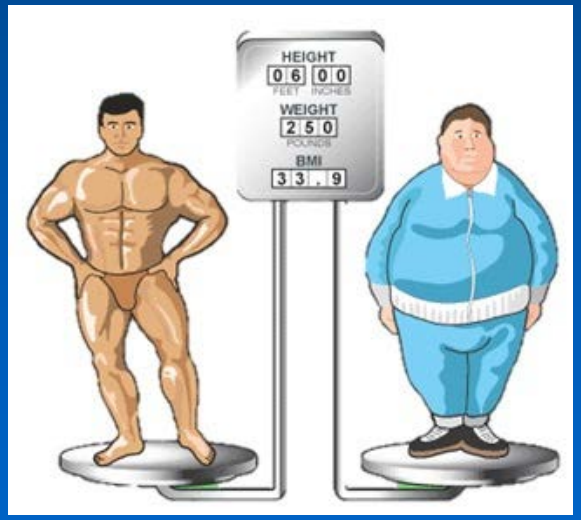
# I. Weight Management

- Scope of the Problem:
  - Approximately 40-60% of breast cancer survivors in the US are over weight.
  - The percentage of overweight and obese adults and children has been steadily increasing during the last two decades, and it is estimated that one third of US adults are obese.
  - If the current trends continue, 43 percent of U.S. adults will be obese and obesity spending will quadruple to $344 billion by 2018


1. Flegal, K.M., et al., *Prevalence and trends in obesity among US adults, 1999-2008.* Jama, 2010. **303**(3): p. 235-41.
2. Jackson SE, et al., *Weight Loss and Mortality in Overweight and Obese Cancer Survivors: A Systematic Review.* PLoS ONE 12(1): e0169173. doi:10.1371/journal.pone.0169173

# Weight Assessment Tools

- Body Mass Index (BMI)
  - Is a broad general measure of weight adjusted for height and often considered an indicator of body 'fatness.'
  - Is not the best indicator of health and wellness because it cannot identify between lean mass and body fat.
- Body weight is a non-specific measure of the patient.
- Decrease in weight in obese patient may not be a positive thing if it skeletal muscle mass that is being lost.



# Weight Assessment in Survivorship

- Are there better tools to help monitor weight and body composition to improve overall patient health?

# Advantages of Using BIS

- BIS technology accurately and quickly measures body composition, specifically fluid and skeletal muscle levels
- Body composition analysis may significantly contribute to optimize current oncology treatment and clinical outcomes and monitor patients after treatment for optimal health (better metric than simply tracking weight or BMI)
- A single tool that is easy to use, non-invasive and cost effective
- BIS technology can help a patient and therapist/MD set objective goals (metrics) for treatment/health that can be measured

# II. Chemotoxocity/III. Sarcopenia

- Chemotoxicity:
- Drug Dosing
  - Currently, chemotherapy is dosed based on BMI
  - Body composition (muscle and fat content) is not taken into account even though drugs are distributed differently among muscle and fat.

# Chemotoxicity/Sarcopenia

- Individuals diagnosed with cancer may experience marked and progressive weight loss, primarily of skeletal muscle.
- The resulting severe depletion of skeletal muscle or sarcopenia is associated with treatment failure, chemotherapy toxicity, and a shorter time to tumor progression related to survival.

Villasenor, A., et al., *Prevalence and prognostic effect of sarcopenia in breast cancer survivors: the HEAL Study.* J Cancer Surviv, 2012. **6**(4): p. 398-406

# Chemotoxicity/Sarcopenia

- Sarcopenia is present in 20-70 % of patients depending on the tumor type.
- 1.5% of total healthcare expenditure for older Americans.
- Estimated US $10.8 billion for men, and $ 7.7 billion for women, in 2000.
- Currently BMI is also used to assess patient health.
- May be able to provide patients with more personalized treatment plans if we can assess muscle and fat.

Villasenor, A., et al., *Prevalence and prognostic effect of sarcopenia in breast cancer survivors: the HEAL Study.* J Cancer Surviv, 2012. **6**(4): p. 398-406

# Body Composition as a Predictor of Toxicity

- Two recent studies used CT scans to assess skeletal muscle mass. [1,2.]
- Low muscle quality and quantity resulted in higher risk of experiencing blood-related toxicities, gastrointestinal side effects, and neuropathy.
- Patients were also twice as likely to be hospitalized.
- Poor body composition metrics are significantly associated with increased treatment related toxicities.

1. Shachar, S.S., et al., *Skeletal Muscle Measures as Predictors of Toxicity, Hospitalization, and Survival in Patients with Metastatic Breast Cancer Receiving Taxane-Based Chemotherapy.* Clin Cancer Res, 2017. **23**(3): p. 658-665.
2. Shachar, S.S., et al., *Body Composition as a Predictor of Toxicity in Patients Receiving Anthracycline and Taxane Based Chemotherapy for Early Stage Breast Cancer.* Clin Cancer Res, 2017.

# Sarcopenic Obesity

- Identifying patients with muscle loss has become increasingly difficult as 40-60 % of cancer patients are overweight or obese, even in the setting of metastatic disease.
- A review of 14 studies demonstrated lack of consistency with measurement tools used to assess sarcopenic obesity
- Implications include higher risk of dose-limiting toxicity, surgical complications, physical disability, and shorter survival.


1. Carneiro, I.P., V.C. Mazurak, and C.M. Prado, *Clinical Implications of Sarcopenic Obesity in Cancer.* Curr Oncol Rep, 2016. **18**(10): p. 62.
2. Ryan, A.M., et al., *Cancer-associated malnutrition, cachexia and sarcopenia: the skeleton in the hospital closet 40 years later.* Proc Nutr Soc, 2016. **75**(2): p. 199-211.

# Current Assessment Tools

| | Assessment | | Pros | Cons |
|---|---|---|---|---|
| Weight Scale | Body Weight |  | Common easy to use tool to assess weight loss | Non-specific |
| CT Scan | Skeletal muscle mass |  | Ability to differentiate fat from muscle | Invasive (radiation) |

# Chemotoxicity/Sarcopenia

- Are there other/better ‘tools’ to help manage these issues?
  - As discussed, BIS accurately and quickly measures body composition, specifically fluid and skeletal muscle levels
  - Provides a more appropriate body composition metric to help potentially reduce treatment related toxicities
  - Optimally dose patients based upon a better understanding of their body composition

# IV. Bone Density and Content

- Bone Mineral Content (BMC)
  - Total content of all the bone in the body.
- Bone Mineral Density (BMD)
  - Concentration of bone over a specific area.
- Both typically measured by Dual X-Ray Absorptiometry (DXA) with BMC reported in grams and BMD reported in $cm^2$.
- In most cases with adults both BMD and BMC decline at the same pace.

# Bone Health

- It is well documented that cancer treatment affects bone health.
- Chemotherapy and aromatase inhibitors are known to reduce bone density.
- It is recommended that Dual X-Ray Absorptiometry (DXA) scan to assess bone mineral density is performed every 1 – 2 years.
- Evidence available that bioimpedance can be used to assess bone mineral content.
- Bioimpedance may not entirely replace the traditional clinical diagnosis using DXA, but may allow an easy to use, monitoring tool for changes in BMD in order to evaluate whether a certain treatment has been improving the medical condition of the subject between DXA tests.

Hadji, P., et al., *Management of Aromatase Inhibitor-Associated Bone Loss (AIBL) in postmenopausal women with hormone sensitive breast cancer: Joint position statement of the IOF, CABS, ECTS, IEG, ESCEO IMS, and SIOG.* J Bone Oncol, 2017. 7: p. 1-12.

# Conclusions

- BIS technology may be a useful tool in cancer survivorship by:
  - Accurately and quickly measuring body composition, specifically fluid and skeletal muscle levels
  - Providing body composition analyses that may significantly contribute in optimizing current oncology treatment and clinical outcomes
- Provides a single tool that is easy to use, non-invasive and cost effective

# Conclusions

- Trials and studies being implemented to document the practical role of BIS in cancer survivorship:
  - Currently assessing body composition for long-term survivorship goals/recommendations
  - Future directions:
    - Chemotoxicity/Sarcopenia: How to use information to better dose patients and/or provide nutritional/health recommendations
    - Bone Density monitoring adjunct in patients receiving long-term anti-estrogen/androgen therapies