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Use of Dual-Energy X-Ray Absorptiometry to Assess Soft Tissue Composition in Breast Cancer Survivors With and Without Lymphedema

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Abstract

Background: In patients with lymphedema (LE), in addition to hand dominance, between-group comparisons of interlimb soft tissue differences need to account for differences in whole-body adiposity, measured directly by dual energy X-ray absorptiometry (DXA) or indirectly by body mass index. No study has evaluated the effects of hand dominance and whole-body adiposity on limb composition in patients with LE. This study's purpose was to compare soft tissue composition of affected and unaffected limbs of women with breast cancer, who did and did not have LE, controlling for dominance and percent body fat.

Methods and Results: Whole-body DXA scans were acquired and included measures of percent body fat, upper limb total mass, upper limb fat mass, and upper limb fat-free mass. Participants were classified into one of three groups: women without LE; women with only subjective LE; and women with objective signs of LE at the time of assessment. Differences among the LE groups were evaluated using analysis of variance (ANOVA) and Chi-square analyses. Analysis of covariance (ANCOVA) was used to control for percent body fat and for the affected limb dominance. Compared to women without LE, women with objective signs of LE have greater total limb mass, fat mass, and fat-free mass in their affected limbs, independent of affected side dominance and percent body fat. In addition, the interlimb differences in total mass, fat mass, and fat-free mass were greater for the women with objective signs of LE, compared to the other two groups.

Conclusions: DXA is useful in identifying soft tissue changes in patients with LE. Given that limb circumferences measure only changes in limb volume and that bioimpedance provides estimates of extracellular fluid, DXA has the advantage of being able to estimate the volumes of specific tissues in the limb.

Keywords: lymphedema, dual-energy X-ray absorptiometry, breast cancer, circumference, body mass index

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Introduction

Upper limb lymphedema (LE) is a common complication of breast cancer treatments.[1,2] Initial increases in limb volume associated with LE are due to the accumulation of lymph fluid in the interstitial space. Lymph stasis and the accumulation of excess interstitial proteins create chronic inflammation that contributes to fibrosis and fatty deposition, adding to total limb volume.[3,4] In addition, the increased weight of the affected limb creates a greater mechanical load on the muscle with resultant hypertrophy.[5] Therefore, in patients with chronic LE, increases in total limb volume may be related to increases in fat and muscle, as well as fluid.[5–7] These complex changes in tissue composition may explain why chronic LE is less responsive to conservative treatments, which focus on removal of excess fluid.[8]

In addition to examination of the limb for skin and volume changes,[9] approaches to assess limb volume include bioimpedance analysis (BIA), water displacement, and circumferential measurement.[10] These methods cannot quantify the amount of fat or muscle that contributes to total limb volume. Dual-energy X-ray absorptiometry (DXA) may provide added value because of its ability to evaluate for the presence of excess adipose tissue and changes in lean tissue that contribute to volume increases in LE. DXA estimates tissue composition, including fat mass and fat-free mass.[11–13] Fat mass includes adipose tissue and associated fibroblasts, white blood cells, nerves, and endothelial cells. Fat-free mass is the sum of lean soft tissue and bone mineral components, formed by skeletal and nonskeletal muscle, organs, connective tissue, and bone. Information about fat mass and fat-free mass may increase our understanding of LE phenotypes as well as changes in tissue composition that occur with LE progression.

Only four studies have evaluated for differences in tissue composition in the upper limbs of breast cancer patients with LE using DXA.[5–7,14] Two of these studies compared the lymphedematous arm to the nonlymphedematous arms. Findings included increased fat, lean, and total volume[14] and increased fat, muscle, and bone volume[5] in the affected limb. However, the effects of hand dominance and whole-body adiposity on soft tissue composition were not investigated, nor were interlimb differences in DXA measures compared between women with and without LE.

Hand dominance can contribute to interlimb volume differences in healthy adult women[15] and in women with LE.[16] In a study that used DXA to evaluate the influence of hand dominance and LE severity on soft tissue composition of a lymphedematous limb,[6] 56 women with LE and 44 healthy women were assessed. Compared to healthy controls, controlling for hand dominance, fat, but not lean volume, was greater in the affected limbs of the women with LE. Increases in fat in the affected arm were not related to increases in whole-body adiposity in women with LE.

In a second study of nine women with LE that controlled for hand dominance,[7] DXA data were compared to body mass index (BMI)-matched women without LE ($n=45$). Women with LE had greater total mass and fat mass in their affected limb compared to their unaffected limb. Compared to healthy controls, interlimb differences in total mass and fat mass were higher in women with LE. Women with LE in their nondominant arm had a greater interlimb difference in fat mass than women with LE in their dominant arm.

Generally, women with LE have a higher BMI, a surrogate measure of body fat based on height and weight.[17–19] In addition to hand dominance, between-group comparisons of interlimb soft tissue differences need to account for differences in whole-body adiposity, measured directly by DXA or indirectly by BMI. However, no study has evaluated the effects of hand dominance and whole-body adiposity or BMI on limb composition in patients with LE. Given the potential benefits of having additional information on soft tissue composition to guide interventions for chronic LE, the purpose of this study was to compare soft tissue composition of affected and unaffected limbs of women with breast cancer, who did and did not have LE, controlling for dominance (i.e., side treated being dominant vs. nondominant) and percent body fat. We hypothesized that compared to women without LE, women with objective signs of LE would have greater total limb mass, fat mass, and fat-free mass in their affected limb, independent of dominance and percent body fat.

Materials and Methods

Study design and participants

As part of a larger study, survivors were recruited from the general population in the San Francisco Bay Area. Eligibility criteria included the following: age ≥18 years, unilateral LE related to breast cancer, and ≥6 months after the completion of surgery, radiation therapy, and chemotherapy. Receipt of targeted or hormonal therapies was not an exclusion criterion.

Study procedures

Study was approved by the University of California, San Francisco Institutional Review Board. All the women provided written informed consent. Compression garments were removed 2 hours before testing. Demographic and clinical information, including history of LE, were collected by questionnaire.

Objective measures

Limb circumference. Circumferential measurements of the upper limbs were done at 10-centimeter intervals from the wrist up to a total distance of 40 cm proximally. Limb volume was calculated using the formula for a truncated cone.[20] Interlimb differences were calculated as affected limb volume—unaffected limb volume.

Bioimpedance. Inbody 770 multifrequency BIA device was used to measure impedance. Bioimpedance measurements were taken with the women standing on the device platform. The 5 kHz impedance ratio (unaffected/affected limb) was calculated from the output.

Soft tissue composition. Whole-body DXA scans were acquired on a Hologic Discovery/W (Hologic, Inc., Marlborough, MA; software version 13.5.2.1[21]). Measures were taken in an anterior/posterior view with the participant supine and with limbs straight and not touching the body. Measures included were as follows: percent body fat, upper limb total mass, upper limb fat mass, and upper limb fat-free mass.

Data analysis

Participants were classified into one of three groups: women without LE (i.e., no self-reported history of LE and no evidence of LE at the time of the assessment); women with only subjective LE (i.e., self-report of past or current history of LE, but no evidence of LE at the time of the assessment); and women with objective signs of LE at the time of the assessment. Objective cases of LE were defined by one of two thresholds: affected–unaffected limb volume difference of ≥200 mL or a bioimpedance ratio of ≥1.139 if the dominant upper limb was affected or ≥1.066 if the nondominant upper limb was affected.[16]

Descriptive statistics were calculated for demographic and clinical characteristics and DXA measures. Differences among the LE groups were evaluated using analysis of variance (ANOVA) and chi-square analyses. Analysis of covariance (ANCOVA), based on estimated means and standard errors, was used to control for percent body fat and for the affected limb dominance. Bonferroni correction was used for multiple comparisons of outcomes. Effect sizes were calculated for between-group differences (i.e., Cohen's *d*).[22] Analyses were done using SPSS version 23 (IBM Corporation, Armonk, NY).

Results

Demographic and clinical characteristics

Compared to women without LE, women with objective LE had a higher weight, BMI, total body fat percent, and bioimpedance ratio and greater interlimb volume difference. In addition, they had higher number of lymph nodes removed and were more likely to have had a mastectomy, axillary lymph node dissection, and adjuvant chemotherapy. Compared to women with subjective LE, women with objective LE had greater interlimb volume difference, higher bioimpedance ratio, and higher number of lymph nodes removed. Compared to women without LE, women with subjective LE had higher number of lymph nodes removed. No differences were found among the groups in limb dominance or affected side or the numbers of women who reported that their dominant limb was their affected limb (Table 1).

Differences in DXA outcomes for affected and unaffected limbs

For the affected limbs, compared to women without LE, women with objective LE had greater upper limb total mass, fat mass, and fat-free mass. Compared to the women with only subjective LE, women with objective LE had greater fat-free mass. No difference was found between the only subjective LE and no LE groups. For the unaffected limb, compared to women without LE, women with objective LE had greater upper limb fat mass in the unadjusted analysis. When controlling for percent body fat and dominance, no difference was found between the groups (Table 2).

Interlimb differences in DXA outcomes

Compared to women without LE and women with only subjective LE, interlimb differences for all DXA measures were greater in women with objective LE (Table 3).

Effect sizes

Effect sizes were calculated to evaluate for clinically meaningful between-groups differences. In terms of the affected limb, effect sizes for the no LE group compared to the objective LE group were as follows: 0.57 for fat-free mass, 0.76 for fat mass, and 0.78 for total mass. Effect sizes for the objective LE group compared to only subjective LE group were as follows: 0.48 for fat-free mass, 0.30 for fat mass, and 0.43 for total mass. Effect sizes for the only subjective LE group compared to the no LE group were 0.08 for fat-free mass, 0.43 for fat mass, and 0.32 for total mass.

In terms of interlimb differences, effect sizes for the no LE group compared to the objective LE group were as follows: 0.76 for fat-free mass, 1.38 for fat mass, and 1.17 for total mass. Effect sizes for the objective LE group compared to the only subjective LE group were as follows: 0.68 for fat-free mass, 1.00 for fat mass, and 0.92 for total mass. Effect sizes for the no LE group compared to the only subjective LE group were as follows: 0.76 for fat-free mass, 1.38 for fat mass, and 1.17 for total mass.

Discussion

This study extends previous work that compared upper limb soft tissue composition in women with and without unilateral upper limb LE.[5–7,14] Our findings support the hypothesis that compared to women without LE, women with objective signs of LE have greater total limb mass, fat mass, and fat-free mass in their affected limbs, independent of affected side dominance and percent body fat. In addition, the interlimb differences in total mass, fat mass, and fat-free mass were greater for the women with objective signs of LE, compared to the other two groups.

Total mass

Consistent with previous studies,[5–7,14] total mass (fat mass+fat-free mass) was greater in the affected limb of women with objective signs of LE, when unaffected limbs were used as comparator and compared to women without LE. In our study, this increase appears to be due to increases in both fat mass and fat-free mass. For the unaffected limb, adjusting for dominance and percent body fat resulted in no difference between the groups. In addition, interlimb differences between women with objective LE and the other two groups were independent of dominance and percent body fat, which suggests that the interlimb differences in total mass are more closely associated with the presence of LE than whole-body adiposity and affected limb dominance.

Fat mass

In our study, differences were found in fat mass in the affected limb between women with objective LE and those without LE, which were not associated with percent body fat or hand dominance, suggesting that these differences are more closely associated with the presence of LE than with differences in whole-body adiposity or limb dominance. Similarly, interlimb differences in fat mass were independent of the influence of percent body fat or hand dominance. These results contrast with findings from studies that found interlimb fat differences were influenced by affected limb dominance.[6,7] Differences in participant characteristics

Table 1. Differences in Demographics and Clinical Characteristics Among the Lymphedema Groups

Characteristic	*Women without LE (1)* n = *158 Mean (SD)*	*Women with only subjective LE (2)* n = *46 Mean (SD)*	*Women with objective signs of LE (3)* n = *52 Mean (SD)*	*Statistics*
Age (years)	61.0 (12.2)	58.9 (9.8)	62.8 (9.0)	$F = 1.50$, $p = 0.226$
Weight (kg)	68.3 (14.3)	70.7 (11.9)	73.9 (13.2)	$F = 3.31$, $p = 0.038$ 3 > 1
Height (cm)	163.3 (7.2)	164.2 (6.8)	163.8 (6.2)	$F = 0.35$, $p = 0.704$
BMI (kg/m^2)	25.6 (4.9)	26.3 (4.7)	27.5 (4.8)	$F = 3.24$, $p = 0.041$ 3 > 1
Total body fat percent from DXA	36.7 (5.3)	38.3 (4.9)	39.2 (5.3)	$F = 5.29$, $p = 0.006$ 3 > 1
Months since diagnosis	96.2 (84.4)	91.0 (80.7)	100.0 (76.4)	$F = 0.14$, $p = 0.866$
Months since surgery	94.1 (85.5)	89.6 (81.4)	98.6 (76.8)	$F = 0.15$, $p = 0.865$
Number of nodes removed	7.2 (7.6)	10.6 (8.0)	12.7 (8.8)	$F = 10.08$, $p < 0.001$ 2 and 3 > 1
Interlimb volume difference (mL)	−11.2 (82.6)	12.9 (108.3)	262.3 (257.7)	$F = 75.05$, $p < 0.001$ 3 > 1 and 2
Affected-unaffected (calculated from circumference measurements)				
Interlimb bioimpedance ratio (inbody at 5 kHz)	0.99 (0.03)	1.00 (0.03)	1.19 (0.15)	$F = 135.88$, $p < 0.001$ 3 > 1 and 2
	n *(%)*	n *(%)*	n *(%)*	
Race				$X^2 = 7.12$,
Asian	20 (12.7)	4 (8.9)	1 (1.9)	$p = 0.524$
Black or African American	5 (3.2)	1 (2.2)	2 (3.8)	
White	122 (77.2)	36 (80.0)	47 (90.4)	
Mixed Ethnic background	8 (5.1)	3 (6.7)	2 (3.8)	
Other	3 (1.9)	1 (2.2)	0 (0)	
Dominant hand				$X^2 = 0.71$, $p = 0.701$
Right	138 (87.3)	39 (84.8)	47 (90.4)	
Left	20 (12.7)	7 (15.2)	5 (9.6)	
Affected side				$X^2 = 2.92$, $p = 0.232$
Right	90 (57)	27 (58.7)	23 (44.2)	
Left	68 (43)	19 (41.3)	29 (55.8)	
Dominant side affected	90 (57.0)	26 (56.5)	22 (42.3)	$X^2 = 3.54$, $p = 0.171$
Nondominant side affected	68 (43.0)	20 (43.5)	30 (57.7)	
Had mastectomy (vs. BCS)	40 (25.6)	18 (39.1)	24 (47.1)	$X^2 = 9.21$, $p = 0.010$ 3 > 1
Had SLNB	116 (75.8)	33 (73.3)	32 (65.3)	$X^2 = 2.09$, $p = 0.351$
Had ALND	57 (38.5)	26 (57.8)	40 (76.9)	$X^2 = 23.97$, $p < 0.001$ 3 > 1
Had whole breast radiation therapy	88 (72.1)	23 (69.7)	33 (76.8)	$X^2 = 0.524$, $p = 0.769$
Had adjuvant chemotherapy	79 (64.8)	26 (78.8)	38 (88.4)	$X^2 = 9.69$, $p = 0.008$ 3 > 1
Had neoadjuvant chemotherapy	27 (22.9)	8 (24.2)	9 (20.9)	$X^2 = 0.12$, $p = 0.940$

ALND, axillary lymph node dissection; BCS, breast-conserving surgery; BMI, body mass index; DXA, dual-energy X-ray absorptiometry; LE, lymphedema; SD, standard deviation; SLNB, sentinel lymph node biopsy.

among the studies may contribute to these inconsistent findings. While the distributions of dominant side affected were consistent across studies, the mean BMI for our study participants with objective LE was slightly higher and interlimb volume differences were lower than reported in the two previous studies.[6,7]

Forty-six women in this study were considered subjective-only LE cases. While these women reported a history of LE, they were not an objective case because either their LE had improved or their objective measures of LE were below our diagnostic threshold. Interlimb differences for the women with only subjective LE and those without LE were similar. However, women with objective signs of LE demonstrated significant interlimb differences compared to women with no or only subjective LE. These findings suggest the importance of managing LE early to prevent the associated soft tissue changes with persistent LE.

Preclinical studies provide support that if untreated, LE worsens and becomes chronic. Chronic LE is associated with inflammation, skin thickening, and abnormal fibroadipose

Table 2. Differences in Dual X-Ray Absorptiometry Measures for the Upper Limbs Among Women in the Lymphedema Groups

DXA measure	*Women without LE (1)* n = *158* *Mean (SD)* *Estimated mean (SE)*[a]	*Women with only subjective LE (2)* n = *46* *Mean (SD)* *Estimated mean (SE)*[a]	*Women with objective sign of LE (3)* n = *52* *Mean (SD)* *Estimated mean (SE)*[a]	*Statistics (ANOVA)*	*Statistics controlling for percent body fat and dominance (ANCOVA)*
Affected limb					
Total mass (g)	3687.7 (817.2)	3956.3 (906.0)	4332.3 (857.1)	$F = 11.79$	$F = 8.10$
(fat free+fat)	3752.3 (55.2)	3877.3 (101.8)	4205.8 (97.0)	$p < 0.001$	$p < 0.001$
				3 > 1	3 > 1
Fat mass (g)	1544.10 (534.0)	1781.6 (624.9)	1956.5 (555.8)	$F = 11.90$	$F = 7.29$
	1608.7 (27.9)	1714.1 (51.4)	1819.9 (49.0)	$p < 0.001$	$p = 0.001$
				2 and 3 > 1	3 > 1
Fat-free mass (g)	2143.6 (398.6)	2174.7 (412.2)	2375.9 (428.2)	$F = 6.445$	$F = 7.27$
(BMC+lean)	2143.6 (31.6)	2163.2 (58.3)	2385.9 (55.6)	$p = 0.002$	$p = 0.001$
				3 > 1 and 2	3 > 1 and 2
Unaffected limb					
Total mass (g)	3733.4 (863.4)	4004.0 (892.2)	4014.7 (826.6)	$F = 3.12$	$F = 0.53$
(fat free+fat)	3810.1 (57.2)	3933.4 (105.4)	3844.1 (100.5)	$p = 0.046$	$p = 0.592$
				Pairwise NS	
Fat mass (g)	1573.3 (566.4)	1800.7 (667.4)	1796.3 (565.8)	$F = 4.47$	$F = 1.07$
	1642.9 (29.9)	1732.4 (55.1)	1645.4 (52.6)	$p = 0.012$	$p = 0.346$
				3 > 1	
Fat-free mass (g)	2160.0 (417.2)	2203.4 (368.8)	2218.4 (388.4)	$F = 0.507$	$F = 0.19$
(BMC+lean)	2167.2 (32.2)	2200.9 (59.3)	2198.7 (56.6)	$p = 0.603$	$p = 0.826$

Note: dominance refers to dominant side = affected side yes/no.
[a]Estimated mean (SE) used for analysis of percent body fat and dominance covariance.
ANCOVA, analysis of covariance; ANOVA, analysis of variance; BMC, bone mineral content; NS, not significant; SE, standard error.

tissue in the affected limb.[4,23] Fat deposition is considered a distinguishing clinical characteristic of chronic LE. In a mouse tail ablation study,[24] lymphatic obstruction and stasis resulted in significant fat deposition in the subcutaneous tissue of the tail, as a result of hypertrophy and increased numbers of adipocytes. In addition, lymphatic stasis may result in the increased expression of fat differentiation markers.[24–26] If subjective LE or early LE is successfully managed to the point that no objective signs are evident, it may be possible to prevent the progression to fatty deposition.

Fat-free mass

Our findings of increased fat-free mass in the affected limbs of women with objective LE are consistent with some,[5,7,14] but not all[6] previous studies. DXA fat-free mass values include bone mineral mass, skeletal muscle, and connective tissue. In this study, the greater fat-free mass in affected limbs in women with objective LE could be related to any or all of these components. While we did not evaluate for bone mineral content; in another study,[4] greater bone

Table 3. Differences in Dual X-Ray Absorptiometry Measures Between Affected and Unaffected Limbs Among the Lymphedema Groups (Affected–Unaffected)

DXA measures	*Women without LE (1)* n = *158* *Mean (SD)* *Estimated mean (SE)*[a]	*Women with only subjective LE (2)* n = *46* *Mean (SD)* *Estimated mean (SE)*[a]	*Women with objective sign of LE (3)* n = *52* *Mean (SD)* *Estimated mean (SE)*[a]	*Statistics (ANOVA)*	*Statistics controlling for percent body fat and dominance (ANCOVA)*
Interlimb difference	–45.7 (278.6)	–47.7 (395.3)	317.6 (396.4)	$F = 25.47$	$F = 45.91$
in total mass (g)	–57.8 (22.1)	–56.0 (40.8)	361.7 (38.9)	$p < 0.001$	$p < 0.001$
				3 > 1 and 2	3 > 1 and 2
Interlimb difference	–29.3 (115.7)	–19.1 (170.9)	160.2 (187.6)	$F = 35.33$	$F = 44.07$
in fat mass (g)	–34.2 (11.1)	–18.3 (20.4)	174.5 (19.5)	$p < 0.001$	$p < 0.001$
				3 > 1 and 2	3 > 1 and 2
Interlimb difference	–16.4 (218.2)	–28.7 (292.6)	157.5 (253.9)	$F = 11.24$	$F = 24.25$
in fat-free mass (g)	–23.6 (15.6)	–37.7 (28.7)	187.2 (27.4)	$p < 0.001$	$p < 0.001$
				3 > 1 and 2	3 > 1 and 2

Note: dominance refers to dominant side = affected side yes/no.
[a]Estimated mean (SE) used for analysis of percent body fat and dominance covariance.

volume was found in the affected limb of women with LE. This increase was hypothesized to be due to the increased weight of the limb resulting in a higher mechanical load on the skeleton, leading to increased bone mass. Similarly, increased fat-free mass may be related to skeletal muscle hypertrophy due to the increased load on the muscles from a heavier limb.

Development of fibrotic tissue in the limb may contribute to increases in limb volume. In a mouse study of LE,[27] lymph stasis resulted in $CD4^+$ T cell inflammation and T helper 2 (Th2) differentiation. In mice, the $CD4^+$ inflammatory response was required for the pathological changes associated with LE, including fibrosis, adipose deposition, and lymphatic dysfunction. to occur.[27] Activated Th1 and Th2 cells release a number of cytokines, which play a key role in modulating inflammatory responses[28] and may be involved in the development of LE and the fibroadipose changes seen in chronic LE. $CD4^+$ Th2 cells promote the production of profibrotic cytokines and growth factors, including transforming growth factor beta 1 (TGF-β1), IL-4, and IL-13.[29] TGF-β1, a cytokine released by many types of immune cells, is known to regulate the response of fibroblasts to injury, as well as the development of fibrosis. TGF-β1 plays a key role in connective tissue remodeling, scar formation, and fibrosis.[30,31]

The pathogenesis and progression of LE are complex. Identification of multifactorial components associated with increases in limb volume may increase our ability to identify phenotypic subtypes of LE and provide targeted LE interventions to improve outcomes. In addition, DXA could be used in future longitudinal studies of LE to evaluate the timing, progression, and mechanisms associated with tissue composition changes.

Clinical relevance

For the affected limb, effect sizes were in the moderate to large range for differences between women with objective LE and women with no LE. The largest effect sizes were for total mass and fat mass, as well as for interlimb differences between women with objective LE. Given total mass and fat mass have the largest effect sizes, these two parameters may be clinically meaningful and sensitive criteria for diagnosis of LE and intervention outcomes.

Chronic and more severe cases of LE are characterized by changes in the composition of the subcutaneous tissues that become more fibrotic and have an increase in fat deposition.[4] These changes make LE less responsive to treatments directed at reducing volume. Current clinical staging of cancer-related LE relies on clinical history and physical examination of the skin and of limb volume changes.[32] Measurements of limb volume by circumference and BIA do not provide a detailed evaluation of the presence of fluid, fat, or fibrous tissue in the skin and subcutaneous tissues due to LE. DXA provides information about changes in soft tissue composition, including changes in adipose tissue. It can be used in combination with volume measures to obtain a more complete picture of the changes associated with LE. The current LE stages[33] refer to the external appearance of the limb and do not account for the soft tissue composition and fibroadipose changes within the limb. If women are obtaining DXA scans to evaluate for osteoporosis following breast cancer treatment, a whole-body DXA scan may provide useful information on the soft tissue composition of the upper limbs for women at risk for LE progression.

Study limitations

One limitation of this study is that we did not include the hand in our assessment of LE. Women whose LE was only in the hand may not have been included in the objective LE group. However, a strength of this study was the use of only subjective LE as one classification. This approach allowed us to capture milder cases of LE for this analysis. While we did compare our LE groups to women without LE, we did not compare our LE patients to noncancer controls. In addition, we did not consider the effects of exercise or fitness levels on the study outcomes. For example, we did not collect information on resistance training, which may improve tissue composition in the affected limb. Finally, this cross-sectional study was unable to address questions related to the progression and mechanisms underlying the differences in tissue composition. These limitations warrant consideration in the design of future studies to evaluate for LE progression and timing of and predictors of these soft tissue composition changes.

Conclusions

DXA is useful in identifying soft tissue changes in patients with LE. Given that limb circumferences measure only changes in limb volume and that bioimpedance provides estimates of extracellular fluid, DXA has the advantage of being able to estimate the volumes of specific tissues in the limb. Our results, controlling for limb dominance and percent body fat, suggest that LE following breast cancer treatment is associated with increases in affected limb total mass, fat mass, and fat-free mass in the affected arms of women with LE.

Author Disclosure Statement

No competing financial interests exist.

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