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ASSESSING UNILATERAL ARM LYMPHEDEMA STATUS USING INTERARM TISSUE DIELECTRIC CONSTANT RATIOS

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ABSTRACT

Early detection of early-stage lymphedema resulting from breast cancer treatment enables prompt intervention and can potentially slow disease progression. To support this, various methods have been developed that use quantitative criteria sensitive to excess tissue fluid, which is a hallmark of lymphedema. One such method involves measuring the dielectric constant (TDC) of arm tissue in both the at-risk and contralateral arms to calculate their ratio. This communication aims to estimate what constitutes an interarm TDC ratio likely to serve as a threshold for arm lymphedema. Data from 403 healthy women were used to calculate the ratio of the highest to the lowest forearm TDC values (β). The distribution of β was analyzed, and estimated lymphedema thresholds were calculated as the mean β plus 2.0, 2.5, and 3.0 standard deviations, producing less and more conservative thresholds. Values ranged from approximately 1.15 to 1.20, with only 0.74% of cases exceeding a β value of 1.20. The β values were not affected by age, which ranged from 18 to 87, or body mass index, ranging from 14.7 to 49.9 kg/m². These data represent the most comprehensive reference values available to help physicians and therapists determine appropriate thresholds.

Keywords: Lymphedema detection; Tissue dielectric constant; BCRL; Breast cancer-related lymphedema; TDC; Arm lymphedema thresholds

INTRODUCTION

Lymphedema is a potential complication of breast cancer treatment, with a reported incidence that varies depending on the type and extent of treatment (1-3). When arm lymphedema occurs, it involves the arm on the side of the affected breast and is referred to as the at-risk arm (4). Early detection of incipient lymphedema allows for prompt intervention and thereby potential mitigation of progression. To aid this process, several methods have been developed that use quantitative criteria sensitive to excess tissue fluid, a characteristic of lymphedema. These include calculations of the at-risk arm excess volume relative to the contralateral arm (5-9), bioimpedance spectroscopy (BIS) to measure total arm water (10-13), and measurements of arm tissue dielectric constant (TDC) to assess local tissue water in relation to the same anatomical site on the contralateral arm (14-16).

Prior work using the TDC method to establish thresholds for lymphedema presence measured TDC bilaterally in healthy women and determined the interarm TDC ratio as TDC values in the dominant arm divided by the non-dominant arm (17-19). Because of variability among subjects, some ratio values

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were greater than one, and others were less. With this approach, lymphedema thresholds were considered when the interarm TDC ratio of an at-risk patient exceeded the mean ratio of a healthy population plus N standard deviations. For N = 2.0, 2.5, or 3.0, this includes approximately 95.5%, 98.7%, and 99.7% of cases, respectively, if the ratio is normally distributed. Using this approach, various threshold values have been suggested, ranging from 1.20 to 1.26 (4,19-21).

Although these thresholds have historically been useful indicators, the present work seeks to refine them by enhancing the following two considerations. Firstly, using the dominant/non-dominant ratio, which includes values less than one, may cause the threshold ratio to be lower than it should be. Secondly, the number of women measured in individual prior studies was limited. Thus, the goal of the present study was to reconsider and reanalyze the interarm ratio as the more meaningful ratio of the higher to lower TDC value, defined as b, which is independent of arm dominance, and to compare the resultant thresholds with prior values using the combined data set of a large number of subjects using the actual b-distribution.

METHODS

TDC values measured for potential use in prior studies in which the author was the principal investigator were compiled, combined, and reanalyzed. All studies from which data were drawn were approved by the Nova Southeastern University Institutional Review Board (IRB). The inclusion criteria for this analysis were as follows: (1) the subjects were healthy women with no history of arm lymphedema and at least 18 years old, (2) TDC measurements were made on both anterior forearms in triplicate at corresponding anatomical sites, and (3) TDC measurements were made to an effective measurement depth of 2.5 mm. A total of 403 women satisfied these criteria and were included in the analysis.

The analysis consisted of calculating the interarm TDC ratio, defined for brevity as b = the higher TDC value divided by the lower TDC value, for each subject, independent of which arm (dominant or non-dominant) had the higher TDC value. The arm TDC value was calculated as the average of the triplicate TDC measurements. If both arms had the same TDC value, the ratio was unity (1.00), and all ratios would necessarily be ≥ 1.00. After compiling the 403 interarm TDC ratios, the frequency distribution of β was determined and used to characterize the expected β range for healthy women free of lymphedema.

The goal of this analysis was to provide therapists and treating physicians with a data-driven reference to compare β values obtained from patients at risk of developing breast cancer-related lymphedema (BCRL) with those from a healthy population. The women included in this analysis ranged in age from 18 to 87 years, with an overall mean and standard deviation (SD) of 40.1 ± 19.4 years. They had a body mass index (BMI) ranging from 14.7 to 49.9 kg/m^2, with an overall mean and SD of 25.9 ± 6.0 kg/m^2. Most self-reported as right-handed (94%), although the arm with the greater TDC value was not recorded. Additionally, most identified as White (84%), with 8% reporting as Hispanic, 6% as Asian, and 2% as Black, with percentages rounded to the nearest whole number.

RESULTS

Figure 1 shows the percentage of the 403 healthy women estimated to have an interarm TDC ratio (β) equal to or greater than a specified value. Since β is defined as the ratio of the higher to lower TDC values between the paired arms, the lowest possible value of b is 1.00, meaning 100% of the ratios will be at or above this level. To achieve the most precise resolution, the initial bin size, as depicted in *Figure 1*, is increased by 0.01 in ratio units, with each 0.01 step representing a 1% difference between the TDC values of the paired arms. No healthy subject had a β value exceeding 1.21. The mean and standard deviation of the distribution are 1.052 and 0.046, respectively, with a median value of 1.039. Calculations of the lymphedema threshold β, corresponding to 2.0, 2.5, and 3.0 standard deviations above the

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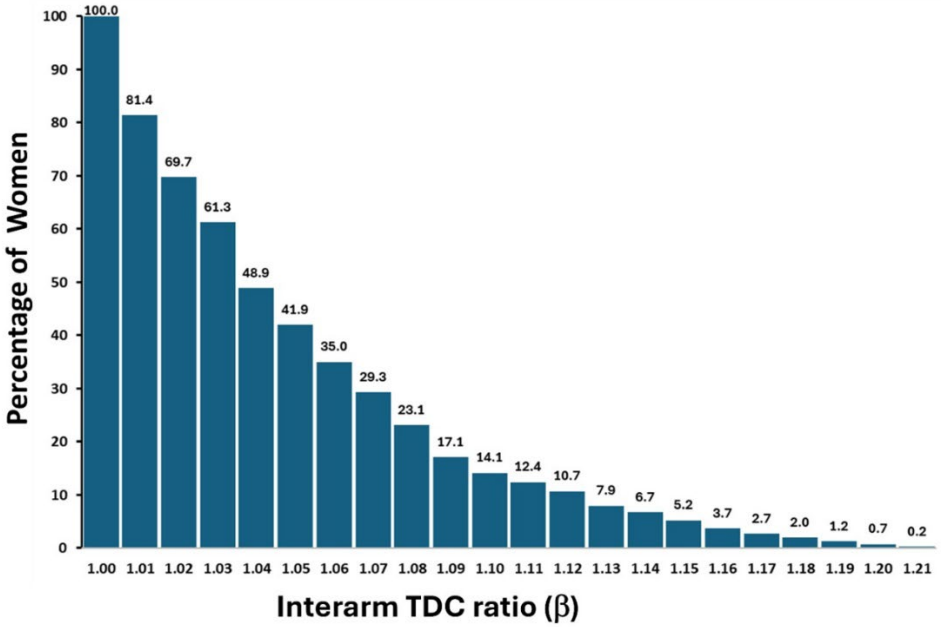

Fig. 1. *Percentage of healthy women estimated to have an interarm ratio greater than the indicated value. Interarm TDC ratios (β) are for 403 healthy women. Numbers on the x-axis indicate endpoints of the bin sizes for β. The first bin size of 1.00 indicates that 100% of healthy women had β values ≥ 1.00. The last bin indicates that 0.20% had a β value greater than 1.21. The numbers above the bars are the exact percentages within each bin. Interarm ratios are determined as the TDC value in the arm that has the higher value divided by the TDC value of the arm with the smaller value.*

mean, give 1.145, 1.168, and 1.191, respectively. The percentages of cases in this healthy group at or above these thresholds are 6.5%, 3.2%, and 1.20%, respectively. Only 0.74% of cases exceed a b value of 1.200.

Figure 2 presents a simplified version of the β distribution, which may be more practical for in-clinic assessment of arm lymphedema risk in patients susceptible to BCRL or for monitoring treatment-related changes in those affected. In this version, the distribution consists of 11 bins, each 0.02 wide, assigned values from 0 to 20. This visualization can facilitate characterizing a patient on a 0-20 scale, where lower numbers suggest a reduced likelihood of lymphedema and higher numbers indicate a greater likelihood. The 0-20 scale also corresponds to the percentage difference related to the given interarm ratio. For example, an interarm ratio of 1.14 translates to a 14% differential, and so forth. During tracking, shifts to lower or higher numbers can indicate changes in treatment effectiveness, with lower values indicating better outcomes than higher ones.

Although the data were collected from subjects with a broad range of BMI values, there was no detectable dependence of β on BMI. This is shown in *Figure 3*, where β values are plotted against BMI, ranging from 14.7 to 49.9 kg/m^2, along with a regression line. The p-value for the regression is 0.828, with a coefficient of determination (R^2) of 0.0001, indicating that β is not significantly affected by BMI. In *Figure 4*, β values are plotted against age, ranging from 18 to 87 years, with a regression line. The p-value for this regression is less than 0.001, and R^2 is 0.039, suggesting that β is slightly related to age, with about 4% of the variation explained by increasing age.

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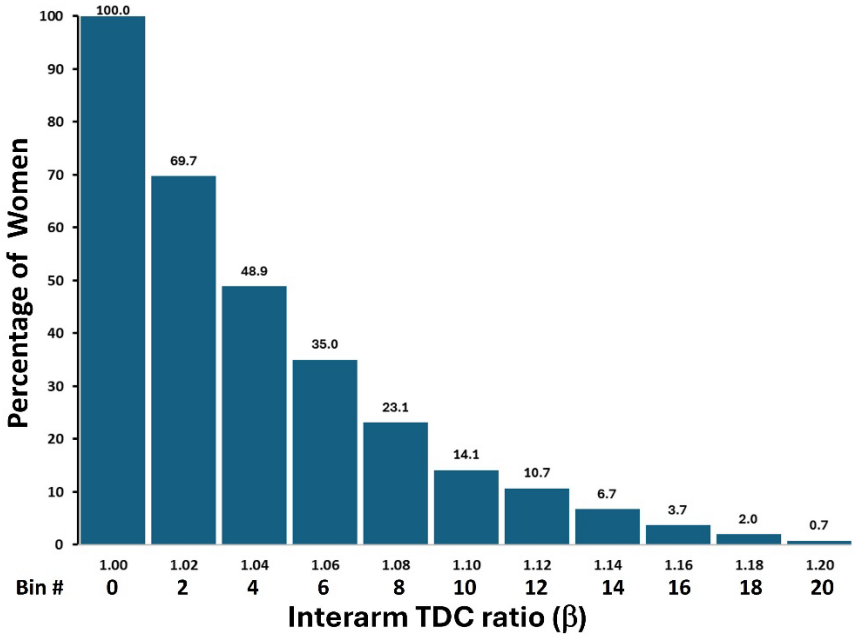

Fig. 2. *Compressed distribution of healthy women with an interarm ratio greater than the indicated value. Interarm TDC ratios (β) are for 403 healthy women, with bin sizes adjusted to yield only 11 groupings ranging from bin 0 to 10. Numbers directly below the bars on the x-axis indicate the endpoints of the bin sizes for β. Bin 0 indicates that 100% of healthy women had β values ≥ 1.00. Bin labeled 20 indicates that 0.70% had a β value greater than 1.20. The numbers 0 through 20 are the percentage interarm differences that correspond to the given interarm ratios. The numbers above the bars are the exact percentages within each bin. Interarm ratios are determined as the TDC value in the arm that has the higher value divided by the TDC value of the arm with the smaller value.*

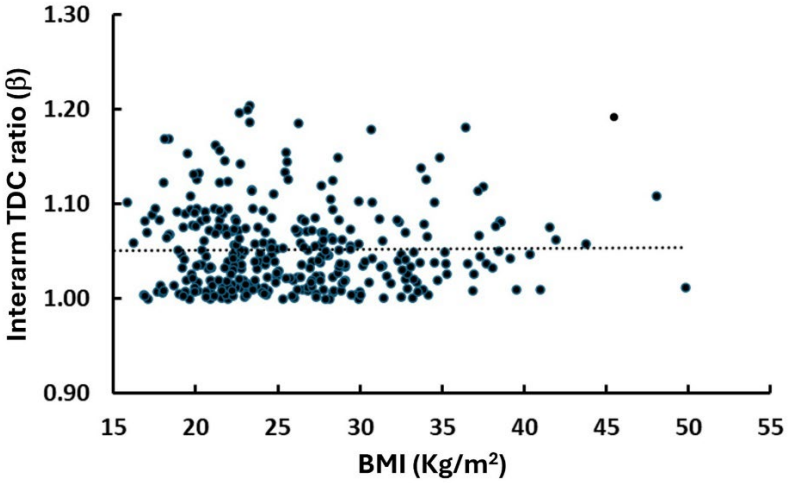

Fig. 3. *Interarm TDC ratio vs. subject BMI. The dotted line is the regression line for the interarm TDC ratio (β) vs. body mass index (BMI). The associated p-value for the regression is 0.828 with a coefficient of determination (R^2) of 0.0001, indicating that β is not significantly dependent on BMI.*

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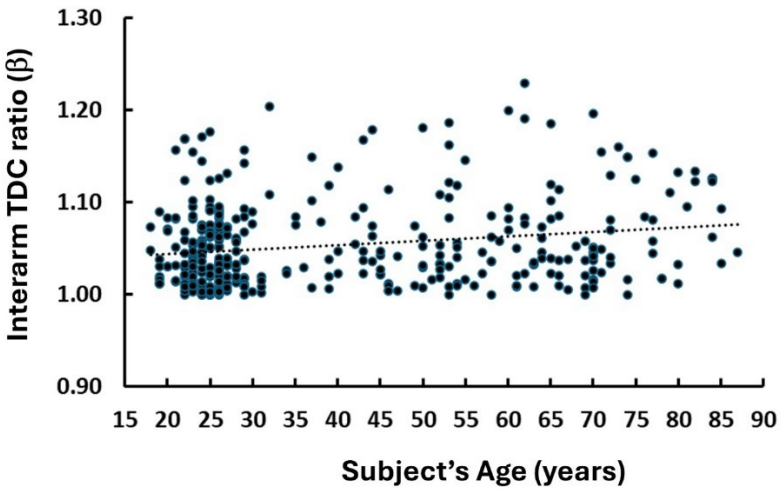

Fig. 4. *Interarm TDC ratio vs. subject age. The dotted line is the regression line for the interarm TDC ratio (β) vs. the subject's age. The associated p-value for the regression is < 0.001, and R^2 is 0.039, indicating that β is slightly dependent on subject age, with about 4% of the variation explained by increasing age. The coefficient of determination for the regression (R^2) is 0.039, indicating that β is not significantly dependent on the subject's age.*

DISCUSSION

The goal of this study was to provide the most accurate current estimate for assessing arm lymphedema based on interarm TDC ratios. The method involved combining all available relevant bilateral TDC data and calculating the distribution of these ratios among 403 healthy women, where each ratio is the higher TDC value divided by the lower. This ratio was defined as β, and thresholds were determined by adding 2.0, 2.5, and 3.0 standard deviations to the overall mean β among these women. The threshold values identified here range from less conservative to more conservative, with the most conservative threshold estimated at a β value of 1.20, for which only 0.74% of women without lymphedema are expected to reach or exceed.

The range of threshold values determined for the present extended population did not differ much from those previously reported, which were based on a smaller number of subjects and used dominant-to-non-dominant arm ratios to calculate interarm TDC ratios (4,19-21). The lowest previously reported threshold ratio was 1.200, which corresponds to the present most conservative estimate. A less conservative threshold estimate based on the present analysis is an interarm ratio of 1.170, corresponding to cases approximately 2.5 SD above the mean. Only 2.7% of healthy women would be expected to have a β -value of 1.170 or greater. The choice of threshold is left to the individual treating physician or therapist, based on their experience and judgment. However, a β -value exceeding 1.170 (corresponding to approximately 2.5 SD above the mean) should indicate a significant difference to the clinicians.

The data presented herein represent the currently most complete reference values to potentially help guide such decisions. In addition to the detailed distribution shown in *Figure 1*, the less detailed representation of *Figure 2*, along with its simple numerical assignment scale, may be a more appropriate classification for some workers in the field.

One limitation of this study that should be considered is that the β-values and any derived lymphedema threshold are estimates based on measurements from women without arm lymphedema. So, in one sense, future validation would be warranted. To some ex-

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tent, some elements of such validation do exist. When interarm ratios are measured in women with unilateral lymphedema, most values reported in the literature, based on at-risk to contralateral arm TDC values, exceed 1.20 (4,22-24). However, further validation studies are warranted to increase confidence.

CONFLICT OF INTEREST AND DISCLOSURE

The author declares no competing financial interests exist.

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