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EXPERIMENTAL

Comparisons of Manual Tape Measurement and Morphomics Measurement of Patients with Upper Extremity Lymphedema

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Background: Lymphedema is a debilitating condition characterized by swelling from lymph fluid exceeding transport capacity. A gold standard for arm measurement is not established, and measurement methods vary. This study evaluates the comparability of the tape measure and Analytic Morphomics in deriving limb circumference measurements in patients with upper extremity lymphedema.

Methods: Fifteen participants with diagnosed upper limb lymphedema were included between July 2013 and June 2017 at Chang Gung Memorial Hospital in Taipei, Taiwan. Affected and unaffected arm circumferences were measured using a flexible tape or morphomic measurement at 10 cm above and below the elbow. Computed tomography scans were standardized, processed, smoothed with a piecewise polynomial algorithm for Analytic Morphomics of arm circumference. Comparative plots, mean percent difference, and adjusted coefficient of determination (R^2) were utilized to compare the consistency of both measurement procedures.

Results: The tape measure and Analytic Morphomics demonstrated consistent measures of arm circumference. On the affected arm, the mean (95% CI) difference in arm circumference between methods was 1.60 cm (0.99–2.20) above, and 0.57 cm (0.23–0.91) below the elbow. Mean percent differences in circumference was 6.65% (SD 3.52%) above and 1.38% (SD 2.11%) below the elbow. The adjusted R^2 for both methods was 94% above and 96% below the elbow.

Conclusions: Analytic Morphomics showed strong consistency with the manual tape measure of arm circumference measurement in those with upper extremity lymphedema. Analytic Morphomics present an opportunity for a precise, granular measurement of limb composition for assessment of disease state and patient planning. *(Plast Reconstr Surg Glob Open 2019;7:e2431; doi: 10.1097/GOX.0000000000002431; Published online 29 October 2019.)*

INTRODUCTION

Lymphedema is a debilitating condition characterized by the abnormal collection of lymph fluid and proteins within the interstitial fluid. Excessive lymph volume surpasses transport capabilities of the lymphatic system, with functional overload resulting in interstitial edema.[1] Lymphedema is common; estimated prevalence in the United States is 1/1,000 persons.[2] Injury to the lymphatic system represents 99% of adult cases; the most disproportionately burdened subpopulation consists of women who previously underwent axillary lymph node dissection and radiation (30% incidence) as treatment for breast cancer.[2,3] Currently, a cure for lymphedema is not

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available, and treatments focus on reducing swelling and discomfort.[4]

Quantitative measurement of lymphedema is necessary for assessment of severity at the time of diagnosis and when evaluating the response to treatment.[5] Assessment of lymphedema severity and progression involves ascertaining circumferential and/or volumetric measurements for comparison to baseline.[6] Variability in measurement methodology is prevalent as there is no "gold standard" for determination in the literature.[7]

Typically, flexible measurement tape is employed to derive circumferential measurements taken at predetermined points (~4–10 cm proximal and distal to the elbow, see Fig. 1).[5,8,9] The tape measure technique is popular due to its low cost, pervasiveness, uniformity, and ease of use.[9] Previous research has demonstrated excellent reliability and validity for manual tape measurement in participants with stage 1 extremity lymphedema. A systematic review demonstrated that among studies using a manual tape measure for measuring lymphedema, a strong pooled intraclass correlation coefficient [0.99 (95% CI, 0.99–0.99)] and a strong pooled interclass correlation coefficient [0.98 (95% CI, 0.98–0.98) with 2.8% weighed standard error of measurement (3.2% variance) were observed.[10] As the tape measure is popular and provides reliable measurements, the manual tape measure method has been utilized as a comparative standard of limb measurement in those with extremity lymphedema.[11,12]

A major challenge facing the management of extremity lymphedema is the development of objective measurements which utilize imaging and clinical findings.[13–15] Analytic Morphomics utilizes semiautomated processing of computed tomography (CT) scans to obtain granular measurements of body composition.[16–18] These measurements can be correlated with clinical outcomes. The Analytic Morphomics process can be applied to these scans to not only obtain limb circumference but also cross-sectional and volumetric measurements of component tissue characteristics including subcutaneous tissue, muscle, and fascia.[19]

The utilization of microsurgical treatments for lymphedema demonstrates the importance of accurate and precise measures of limb circumference and volume.[4,11,20] Without such accuracy and precision, it is difficult to measure disease progression or establish causal longitudinal treatment success. This study aims to evaluate the comparability of the Analytic Morphomics process and the flexible tape measure in deriving limb circumference measurements in a sample of patients with upper extremity lymphedema. Comparability between the Analytic Morphomics measurements and standard tape measurements were assessed statistically.

METHODOLOGY

All retrospectively obtained CT scans of participants (N = 15) were identified as patients of interest in microsurgical treatment. All participants had been diagnosed with unilateral upper limb lymphedema following ablation surgery or radiotherapy for ipsilateral breast cancer at Chang Gung Memorial Hospital (CGMH) in Taiwan, from July 2013 to June 2017. To confirm the diagnosis of lymphedema, all participants had abnormal lymphoscintigraphy demonstrating either partial or total lymphatic obstruction. All scans were secondarily obtained and were not primarily collected for the intention of this study.

Participants were excluded for the following conditions: (1) presence of concomitant systemic or venous cause of limb swelling (eg, heart failure, renal failure, hypoalbuminemia, venous insufficiency, venous thrombosis, or axillary vein stenosis); (2) an episode of acute inflammation or cellulitis during the time of imaging; (3) imaging studies that did not follow study protocol; (4) scans of both the affected and nonaffected limb was not present.

The arm circumferences were measured in centimeters using a standardized flexible tape measure for all patients.

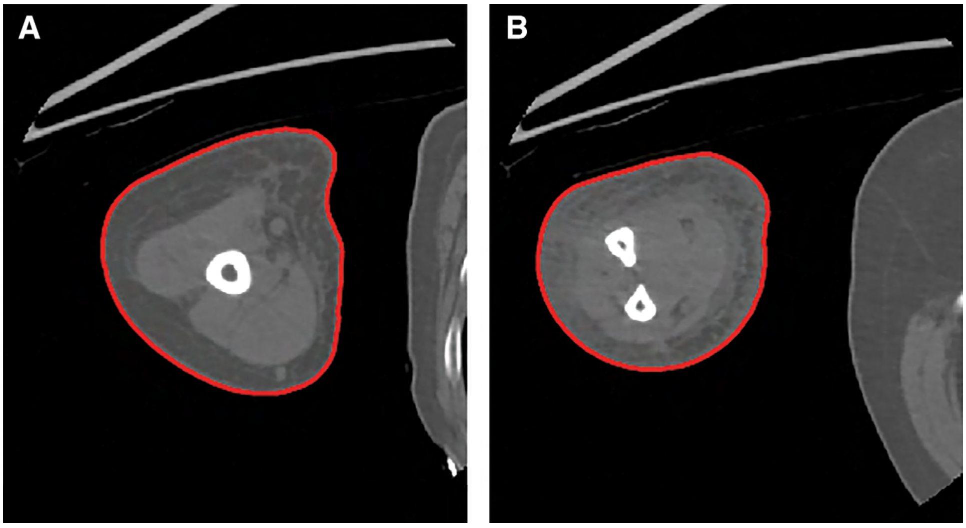

Fig. 1. Standard circumferential measurement points, located 10 cm above (A) and below (B) the elbow on both limbs.

Measurements were performed in the affected and unaffected limbs at 10 cm above (proximal) and below (distal) to the elbow. Figure 1 depicts a typical circumferential measurement locations.

Anatomically comparable measurements of arm circumference were then taken from the CT image volume for each arm. An elbow reference location was placed at the slice containing the medial and lateral epicondyles. Further reference points were placed at the wrist and at the deltoid tuberosity. Thresholding above −205 Hounsfield Units then separated skin from CT background pixels. These skin boundaries were then smoothed with a piecewise polynomial to remove pixel-boundary effects on circumference calculations. Although arm circumference measures were available along the length of the arm, only those at locations 10 cm above and below to the elbow point (Figs. 2 and 3) were used in this study.

Descriptive statistics of the 15 participants were calculated. Patient characteristics were stratified by affected and unaffected arm for all participants (n = 15 participants, 30 arms). Measurements of the distances between 3 arm landmarks are reported: wrist, elbow, and deltoid tuberosity. Differences among the Analytic Morphomics method and the tape measure method were also reported. All distance and comparison measurements were reported as median (interquartile range). As a gold standard is not agreed on in the literature, mean and SD of the percent difference between each method was calculated for both the above- and below-elbow circumferences. To evaluate the proportion of variance explained between both variables, linear regression was performed and the adjusted coefficient of determination (R^2) was calculated. A boxplot was utilized to demonstrate the differences in arm circumference between both measurement types at 10 cm above and below the elbow. Violin plots of arm circumference by measurement type and location, stratified by measurement location, display differences of distribution.

A power analysis revealed that for an $\alpha = 0.05$ and $\beta = 0.80$, a sample size of 12 has appropriate power for a correlation coefficient of 0.75 and a sample size of 7 has appropriate power for a correlation coefficient of 0.95. Given this information, the correlations reported in this study were deemed to have appropriate 80% power at $\alpha = 5\%$.

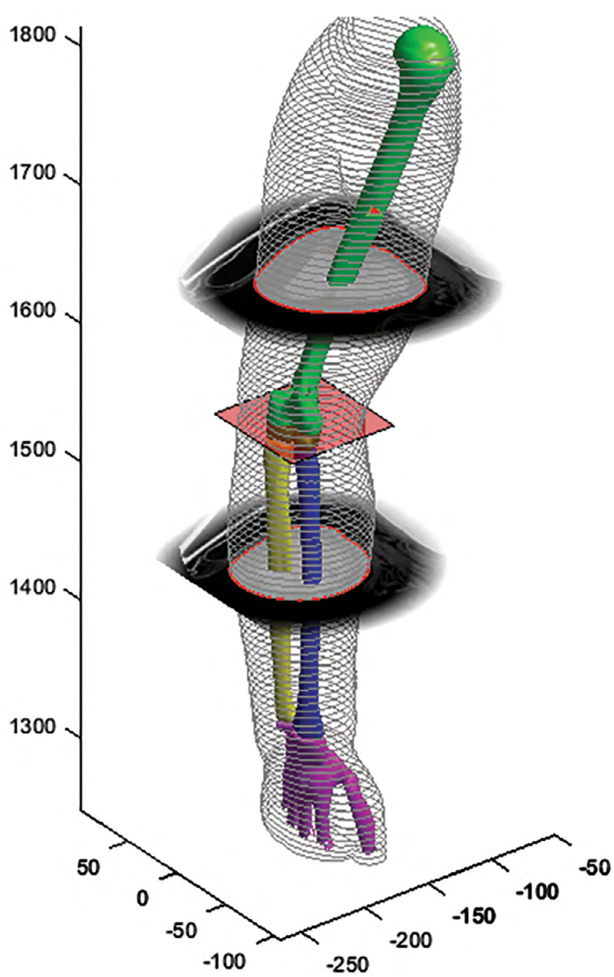

Fig. 2. Cross-sectional view of segmented arm 10 cm below and 10 cm above elbow.

RESULTS

Table 1 shows the consecutive unilateral upper extremity patients' characteristics, tape measurement, and Analytic Morphomics. The patient sample included 9 participants with lymphedema affecting the left arm and 6 participants with lymphedema affecting the right arm. The median age of participants was 58 (interquartile range, 51–65). Median wrist to deltoid tuberosity distance was 36.16 cm (SD 12.95) in affected arms and 35.90 cm (SD 15.37). On the affected arm, the mean (95% CI) difference in arm circumference between methods was 1.60 cm (0.99–2.20) above and 0.57 cm (0.23–0.91) below the elbow. On the affected arm, the mean (95% CI) difference in arm circumference between methods was 2.61 cm (95% CI = 1.98–3.25) above and 0.20 cm (95% CI = −0.34 to 0.73) below the elbow.

The arm circumference measurements from the measuring tape method (blue points) were compared with the Analytic Morphomics method (yellow points) (Figs. 4 and 5). The black bars represent the difference in reported measurement between the 2 techniques. Figure 4 reports the measurements at the point 10 cm below from the elbow. Among the 30 measurements, 29 (97%) had a larger measured circumference reported from the Analytic Morphomics technique relative to the tape measurement technique. The percent difference between both measuring techniques across all participants at the above-elbow point was 6.65% (SD 3.52%). Figure 5 reports the measurements of both techniques 10 cm above from the elbow. Among the 30 measurements, 21 (70%) had a higher measured circumference reported from the Analytic Morphomics technique relative to the tape measurement technique. The percent difference between both measuring techniques across all participants at the below-elbow point was 2.80% (SD 2.11%).

To further demonstrate the consistency of both measures, linear regression was performed and the adjusted coefficient of determination (R^2) was calculated. For the

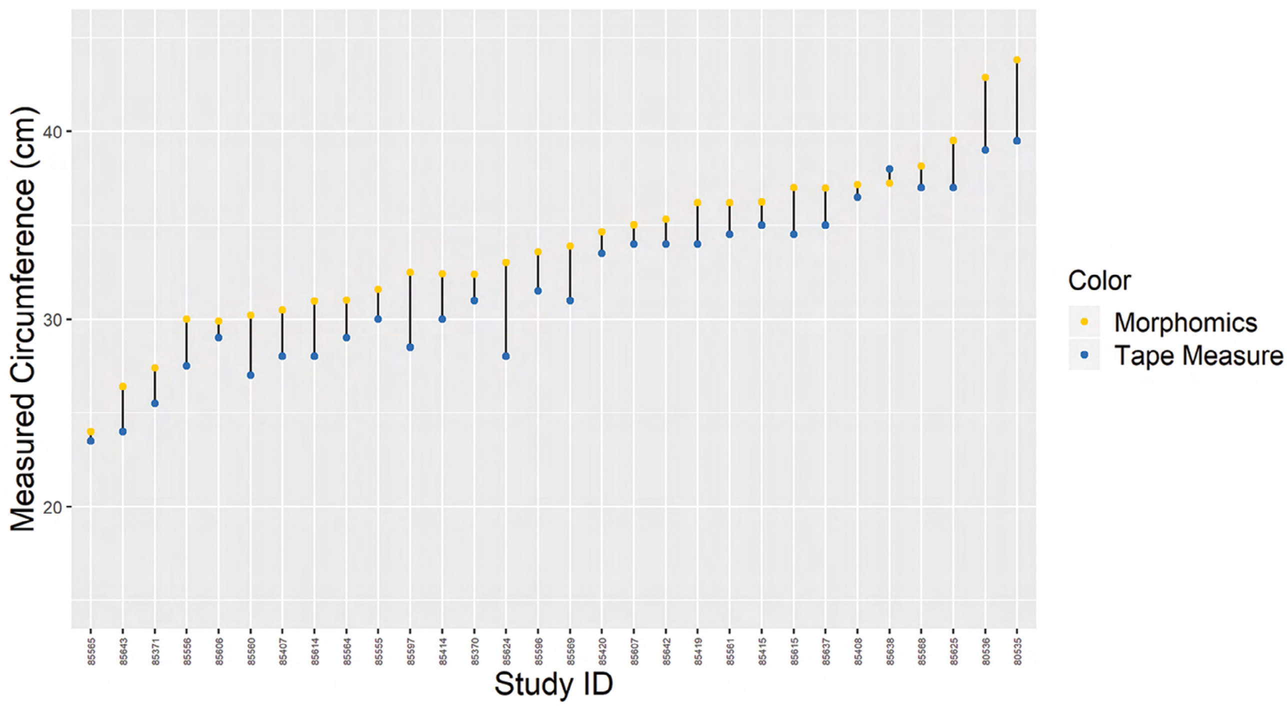

Fig. 3. Three-dimensional model of segmented arm, grey contours represent segmented skin contours.

Table 1. Patient Characteristics

Clinical Characteristic	Affected Side	Unaffected Side	*P*
Left arms (%)	9 (60)	6 (40)	NA
Age	58 (51–65)	58 (51–65)	NA
Difference in measurement (d)	10.40 (12.11)	10.40 (12.11)	NA
Estimated limb measurements			
Elbow to deltoid tuberosity (cm)	36.16 (12.95)	35.90 (15.37)	0.36
Wrist to deltoid tuberosity (cm)	16.27 (5.76)	16.03 (7.65)	0.40
Wrist to elbow (cm)	20.82 (10.49)	20.94 (10.49)	0.58
Above-elbow point circumference			
Analytic Morphomics (cm)	35.93 (3.26)	31.82 (4.61)	<0.01
Tape measure (cm)	34.33 (3.00)	29.20 (4.16)	<0.01
Below-elbow point circumference			
Analytic Morphomics (cm)	29.60 (2.20)	22.74 (2.88)	<0.01
Tape measure (cm)	29.03 (2.22)	23.43 (2.19)	<0.01
Difference in methods, CT versus tape measure			
Circumference above elbow	1.60 (0.99–2.20)	2.61 (1.98–3.25)	<0.01
Circumference below elbow	0.57 (0.23–0.91)	0.20 (−0.34 to 0.73)	<0.01

Reported as mean (SD), frequency (%). Differences reported mean (95% CI). *P* corresponds to paired *t* test.
NA, not applicable.

above-elbow measures, the adjusted R^2 among the manual tape measure and Analytic Morphomics method was 94%. For the below-elbow measures, the adjusted R^2 among the manual tape measure and Analytic Morphomics method was 96%.

A boxplot illustrating the differences of arm circumference between the Analytic Morphomics methods stratified by measurement location is displayed in Figure 6. Both measurement locations were slightly left skewed, demonstrating larger circumference measurements obtained from the Analytic Morphomics technique. The median difference of above-elbow measurements for the Analytic Morphomics technique and the tape measure technique was 2.05 cm, whereas the median difference of below-elbow measurements was 0.35 cm.

Figure 7 demonstrates violin plots of arm circumference by measurement type, stratified by measurement location. At the above-elbow point, the Analytic Morphomics measure appears to be unimodal and normally distributed, whereas the tape measure method appears to be semibimodal. Both measurement methodologies seem to demonstrate bimodal distributions at the below-elbow measurement point.

DISCUSSION

This study aimed to evaluate the consistency of the Analytic Morphomics method and manual tape measure method in individuals with extremity lymphedema. A gold standard for lymphedema measurement does not exist; therefore, a "true measurement" of arm circumference

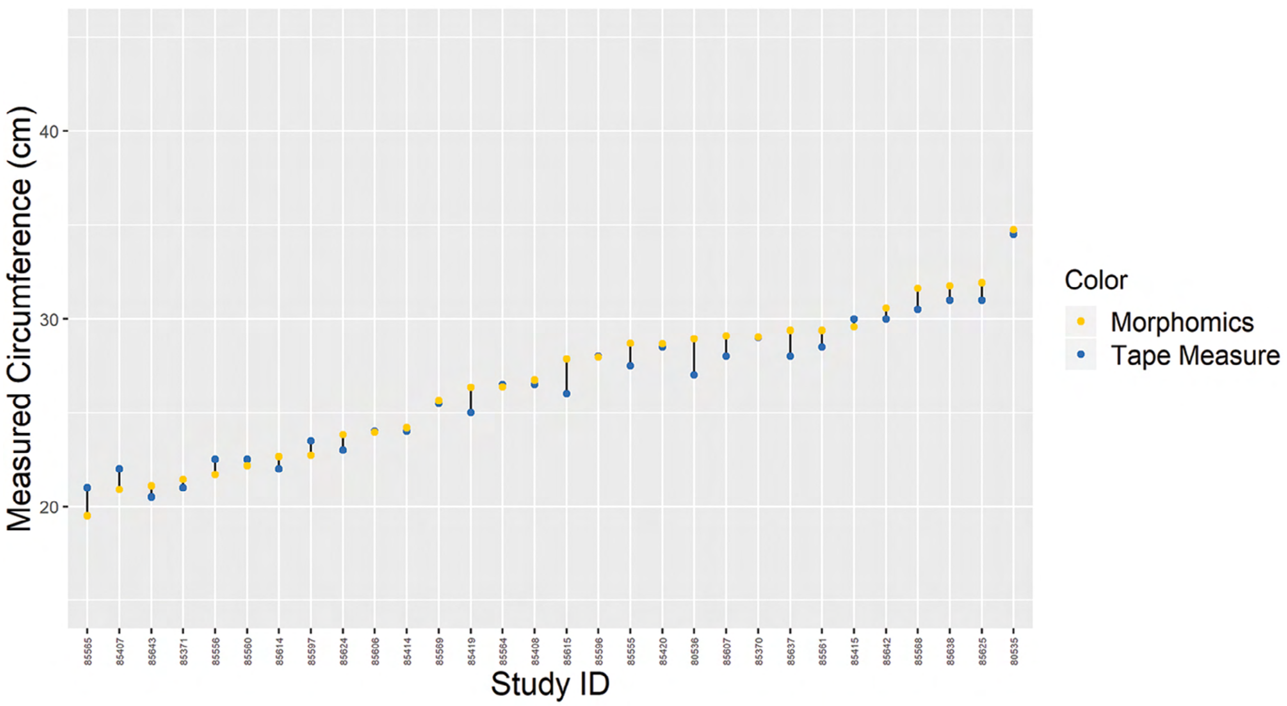

Fig. 4. Comparison of tape measurement and smoothed morphomics measurement at 10 cm below elbow.

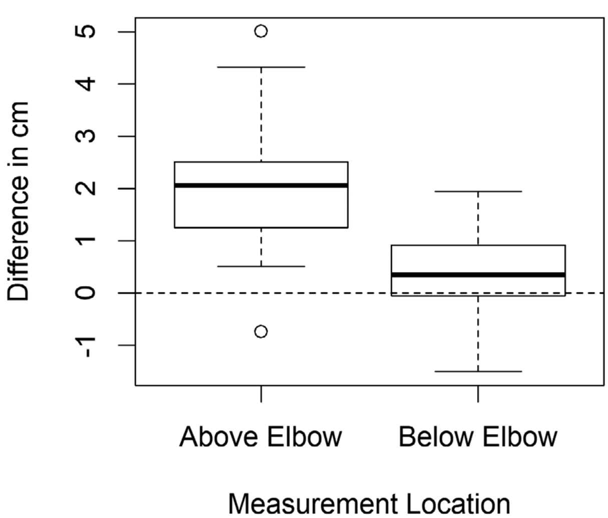

Fig. 5. Comparison of tape measurement and smoothed morphomics measurement at 10 cm above elbow.

and volume is not available. As such, instead of comparing these methods to an unbiased measurement, a comparative analysis demonstrating the similarities in the Analytic Morphomics technique and tape measure technique was performed.

Comparative evaluations show strong consistency among both methods. The percent difference between the 2 methods was 6.65% (SD 3.52%) above the elbow and 2.80% (SD 2.11%) below the elbow, demonstrating minimal error. Further, the adjusted R^2 at both measuring points was very high (adjusted $R^2 = 0.95$ above elbow; 0.96 below elbow, respectively), indicating most of the variation between both techniques were explained by the compared method.

Given the linear concordance between the Analytic Morphomics method and the tape measure method, the 2 cm arm circumference difference above the elbow may be explained by differences in patient position and the physical measurement process. The CT was performed with the patient in the supine position, whereas tape measurements were performed in the upright sitting position with the arms vertical (Fig. 1). The circumference of the arm will alter from fluid displacement due to individual level characteristics such as overall arm volume, gravity, internal blood pressure, and posture.[21–23] With regard to measurement process, the flexible tape measure technique may compress the area of measurement into a more circular form, minimizing the circumference. The tape measure relies on the arm shape being fully convex, and coercing a noncircular arm to circular shapes will result in a slight measurement distortion when compared with the natural shape.[24] With the CT technique, the supine position of the patient and gravity oriented orthogonal to the long axis may flatten the arm and induce folds that increase circumference measured along the skin (Fig. 2). In addition, skin compression can occur with even slight tension, resulting in an artificially smaller circumferential (and volumetric) underestimation of the "true" circumference.[24,25]

Analytic Morphomics provide supplemental information to circumferential measurements in surveilling individual cases of lymphedema. Reoccurring CT measurement can provide insight into change in adiposity, extracellular fluid volume, muscle volume, and localized swelling.[26] The Analytic Morphomics method also provides greater

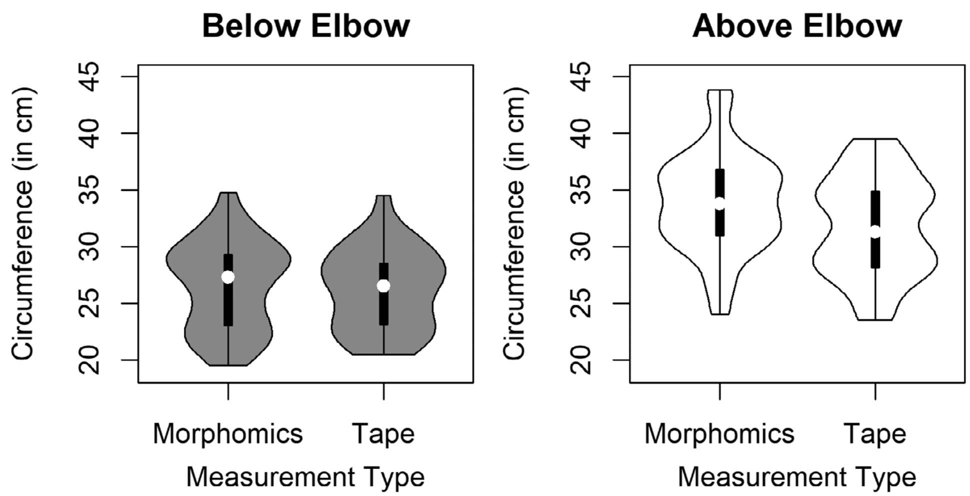

Fig. 6. A boxplot illustrating the differences of arm circumference between the Analytic Morphomics methods stratified by measurement location.

granularity with the potential to provide many cross-sectional measurement points along the entire length of the arm. Further, standardization by arm length can be undertaken by indexing anatomical landmarks, such as the wrist, elbow, and deltoid tuberosity. By indexing the standardized arm, scaling by arm lengths will control for individual variation that limits cross-patient comparability.

This study has a few limitations. CT imaging is currently only performed on patients with extremity lymphedema significant enough to be considered for surgical treatment. As a result, the natural history of soft tissue changes resulting from chronic lymphedema and surgical treatment by vascularized lymph node transfer will only be partially deciphered using the currently available study population. Second, participants were excluded if a CT scan was not present for the affected and nonaffected limbs, which is not a typical procedure. This may have created an additional selection bias. These scans included in this study were secondarily obtained and not collected for the purposes of this study. For financial reference purposes, the cost of a noncontrast CT is (US) $125. In addition, as the sample size is relatively small (n = 15 participants, 30 measurements), extrapolation of the findings obtained in this study to external lymphedema populations may be limited.

CONCLUSIONS

This study reports comparable trends and consistent measurements among Analytic Morphomics and the manual tape measure for circumferential measurements in individuals with extremity lymphedema. Analytic Morphomics present an opportunity for a precise, granular measurement of limb composition, for inference of disease state and patient care.

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