

MEASUREMENT OF SOFT TISSUE COMPLIANCE WITH PRESSURE USING ULTRASONOGRAPHY

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ABSTRACT

Lymphedema is swelling, particularly in the subcutaneous tissues, due to accumulation of lymph. Previous imaging techniques have demonstrated associated structural changes and have been used for evaluating the status of soft tissues. However, the reliability of measurements using ultrasonography has not been evaluated and the ultrasonographic method has been unable to show changes in tissue softness. There is a need to determine if ultrasonography is a reliable technique to assess skin and subcutaneous thickness in the upper extremities with or without pressure and if the measure of compliance in soft tissue thickness is also reliable. Two examiners measured tissue thicknesses using ultrasonography and calculated the compliance with and without pressure on the forearm and upper arm, independently. The intra- and inter-rater cross-correlation coefficients of measuring soft tissue thickness were excellent (>0.75) in the forearm ($p<0.05$). In the upper arm, the reliabilities were fair-to-good. The intraclass correlation coefficients of pressure compliance in the forearm and upper arm were excellent and fair-to-good, respectively ($p<0.05$). This study suggests that measurement of thickness of soft tissues using ultrasonography may be reliable and pressure compliance may reflect tissue softness in the upper extremity.

Keywords: compliance, ultrasonography, lymphedema, soft tissue

Lymphedema is swelling, especially in the subcutaneous tissues, as a result of obstruction of lymphatic vessels or lymph nodes, with accumulation of lymph in the affected region (1,2). The prevalence of lymphedema after surgery for breast cancer has been reported to vary from less than 10% to as much as 50% (3-8). The disorder generally affects the dermis and spares the deeper compartments of the skin (9), and it can become irreversible due to the increased formation of fibrous or adipose tissue (10,11). Successful treatment outcomes for lymphedema after breast cancer surgery have been reported (12-15).

Several measurement tools have been used for determining outcomes following treatment of lymphedema. Clinically, measuring arm circumference with volume calculation is the most popular and convenient method. However, this method cannot evaluate structural changes in the subcutaneous tissues, and errors can be caused by excessive tape-measure pressure on the tissues, inaccurately marked points, and an improper angle measured in relation to the long axis of the limb (9,16). Volumetry using water or an infrared light beam are excellent tools which can give data pertaining to the soft tissue volume automatically (17,18).



Fig. 1. Positioning of subject during soft tissue thickness measurements on the upper arm (A) and forearm (B).

However, volumetry also cannot check the structural changes in tissues, can be time-consuming, and is not suitable for assessing joint movement limitations (9,16).

For measuring the structure and volume of subcutaneous tissues, image analysis has been used. Magnetic resonance imaging (MRI) and computed tomography (CT) have been introduced for the analysis of soft tissues (19-25). MRI can detect enlarged lymph nodes and lymphatic vessels and identify the underlying cause of lymphedema (19). These imaging techniques have been used in evaluating the outcome of lymphedema after CDT (20). However, because these tools are expensive and require time, MRI or CT cannot be offered whenever a patient visits the hospital.

Ultrasonography is a clinically convenient tool, and the examiner can measure the status of soft tissues in the office setting (26,27). The thickness of the cutaneous, epifascial, and subfascial tissue compartments can be measured using ultrasonography (28,29). In addition, fluid collection and fibrosis can be shown with ultrasonography. Because ultrasonography may be a relatively subjective tool in which findings can be affected by the practitioner or pressure, the reliability needs to be evaluated (30). Measuring tissue softness is also an important factor for evaluating the improvement of

lymphedema with treatment. Although imaging techniques are good tools for detecting structural changes in soft tissues, the existing measurements can not reveal changes in the physiologic compliance of soft tissues. To evaluate the change of volume and tissue characteristics simultaneously, a modified imaging technique should be adapted.

The purpose of this study was to determine if simple ultrasonographic measurement is a reliable technique to assess skin and subcutaneous thickness in the upper extremity with or without pressure and if the measurement of compliance in soft tissue thickness is also reliable.

METHODS

Subject Recruitment

Thirteen healthy volunteers were recruited (8 males and 5 females; age range, 26-37yr; mean age, 28.6 3.9yr). Written informed consent was obtained from all subjects. Subjects did not have a history of edema, surgery, or cardiovascular disease.

Measurement with Ultrasonography

Subjects sat on a chair with supination of the left arm, which was placed on the thigh (Fig. 1). The midpoint of the wrist crease, the

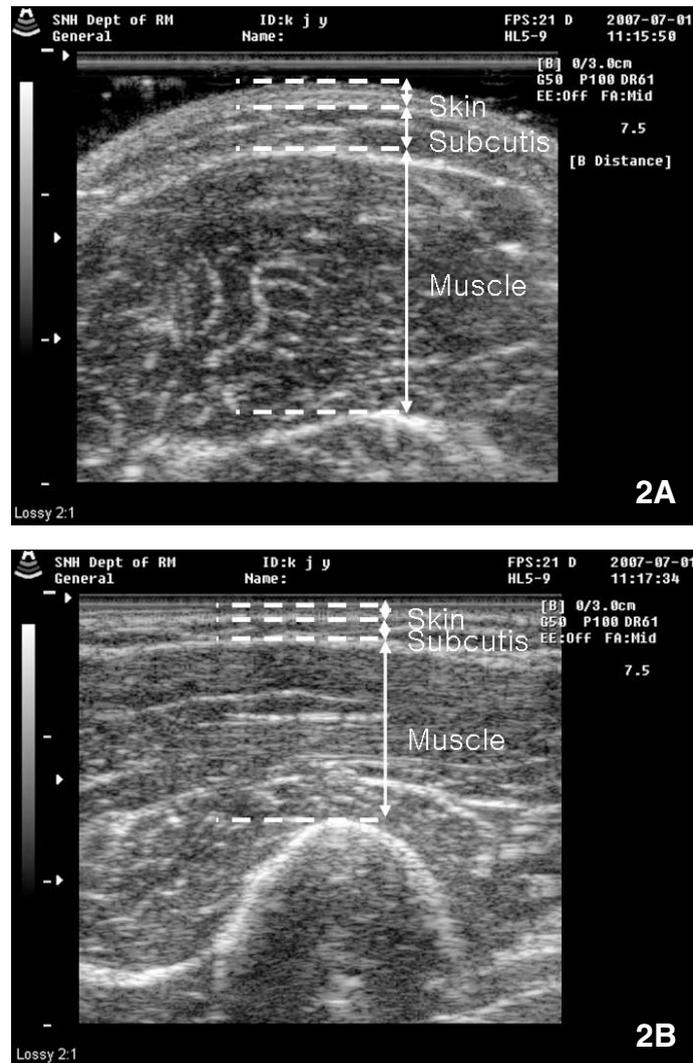


Fig.2. Cross-sectional sonographic images of the upper arm without compression (A) and with maximal compression (B).

midpoint between the medial and lateral epicondyles at the level of the elbow, and the bicipital groove were marked. These three points were connected directly, and the two target areas (below and above the midpoint at the level of the elbow) were finally marked. Soft tissue thickness was measured using an ultrasound unit with a 7.5 MHz transducer (Digital GAIA SA 8800; Medison Co., Seoul, Korea). The gain settings were not changed during the study. Ultrasound gel was applied liberally on the skin, and the probe was

placed transversely on the target areas on the forearm. Avoiding the pressure by the sonographer, the image was captured when the thickness of the gel was at least 1 cm and the soft tissue contour was not distorted (Fig. 2). A two-dimensional image of the soft tissue was captured and thicknesses of the skin, subcutis, and total tissue (skin and subcutis) were measured vertically using the calibrator within the ultrasound unit. Then, the same measurement was performed with maximal pressure. “Maximal compression” was

TABLE 1
Soft Tissue Thickness Measurements with Pressure Using Ultrasound

		Without compression (mm)	Maximal compression (mm)	Compliance (mm)
Forearm	Skin	1.39 ± 0.28	1.16 ± 0.19	0.22 ± 0.26
	Subcutis	3.55 ± 1.58	2.51 ± 1.05	1.05 ± 0.84
	Total	4.94 ± 1.65	3.67 ± 1.06	1.27 ± 0.97
Upper arm	Skin	1.42 ± 0.38	1.02 ± 0.23	0.40 ± 0.21
	Subcutis	3.95 ± 1.71	2.47 ± 0.88	1.49 ± 1.21
	Total	5.37 ± 1.78	3.49 ± 0.89	1.88 ± 1.24

defined as enough compression that additional manually-delivered pressure could not reduce the thickness of the visible soft tissue. The thicknesses of the skin and subcutis in the upper arm were also measured after evaluating the thickness in the forearm. Two sonographers measured the thickness and compliance with pressure on the forearm and upper arm differently; the sonographers had performed ultrasonography for 3 and 9 years. These measurements were carried out twice by each sonographer. A total of 24 data points for each subject were collected with and without pressure in the forearm and upper arm by the two sonographers.

Measurement with Tape

To compare the reliability of the ultrasonographic measure with that of conventional circumference measure, the circumferences of the forearm and upper arm were measured twice at the same sites with tape by each sonographer. Excessive pressure was not applied during measurement of the circumferences. A total of 8 data points for each subject were collected in the forearm and upper arm by two sonographers.

Measurement Parameters

Thicknesses of the skin, subcutis, and total tissues and circumference measurements in the forearm and upper arm were collected for intra- and inter-rater comparisons. Pressure compliance was defined as a change of thickness between the measurement without compression and with maximal compression in the skin and subcutis. To evaluate the error of compliance with the size of arm, we used the difference of compliance between first and second trial in each sonographer and the difference of mean compliance between two sonographers

Data Analysis

All statistical analyses were performed with SPSS/PC+ software (SPSS Inc., Chicago, IL, USA). The intra- and inter-rater reliabilities of measurement were determined using the intraclass correlation coefficient (ICC) with a 95% confidence interval. Coefficients should be accepted as “excellent” when at least 0.75. Values from 0.4 to <0.75 were indicative of fair-to-good reliability. The reliability was poor when the coefficient was <0.4 (31). Spearman’s rho-coefficients were calculated between the circumference with tape and the difference of compliance with sonography.

TABLE 2 ICC of the Soft Tissue Thickness Measurements Using Ultrasound in Forearm				
	Without compression		Maximal compression	
	Intra-rater	Inter-rater	Intra-rater	Inter-rater
Skin	0.812**	0.569*	0.689**	0.534*
Subcutis	0.966**	0.868**	0.963**	0.852**
Total	0.962**	0.900**	0.952**	0.848**

*p<0.05; **p<0.01. Abbreviation: ICC = intraclass correlation coefficient

TABLE 3 ICC of the Soft Tissue Thickness Measurements Using Ultrasound in Upper Arm				
	Without compression		Maximal compression	
	Intra-rater	Inter-rater	Intra-rater	Inter-rater
Skin	0.656**	0.409	0.632**	0.676**
Subcutis	0.968**	0.832**	0.895**	0.609*
Total	0.974**	0.760**	0.904**	0.539*

*p<0.05; **p<0.01. Abbreviation: ICC = intraclass correlation coefficient

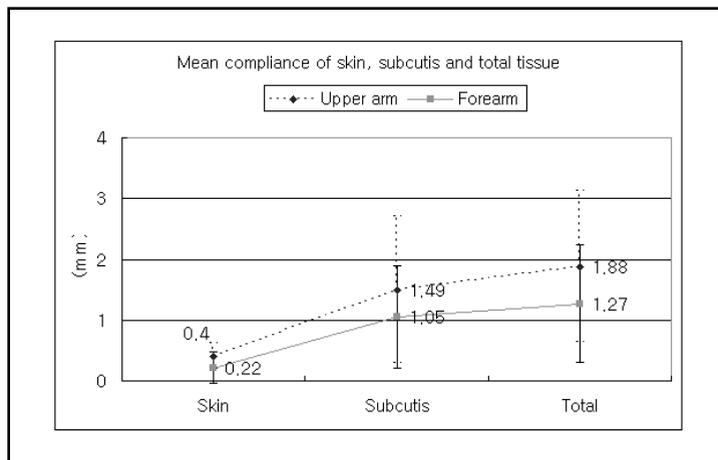


Fig. 3. Mean compliance of skin, subcutis and total tissue in upper extremity.

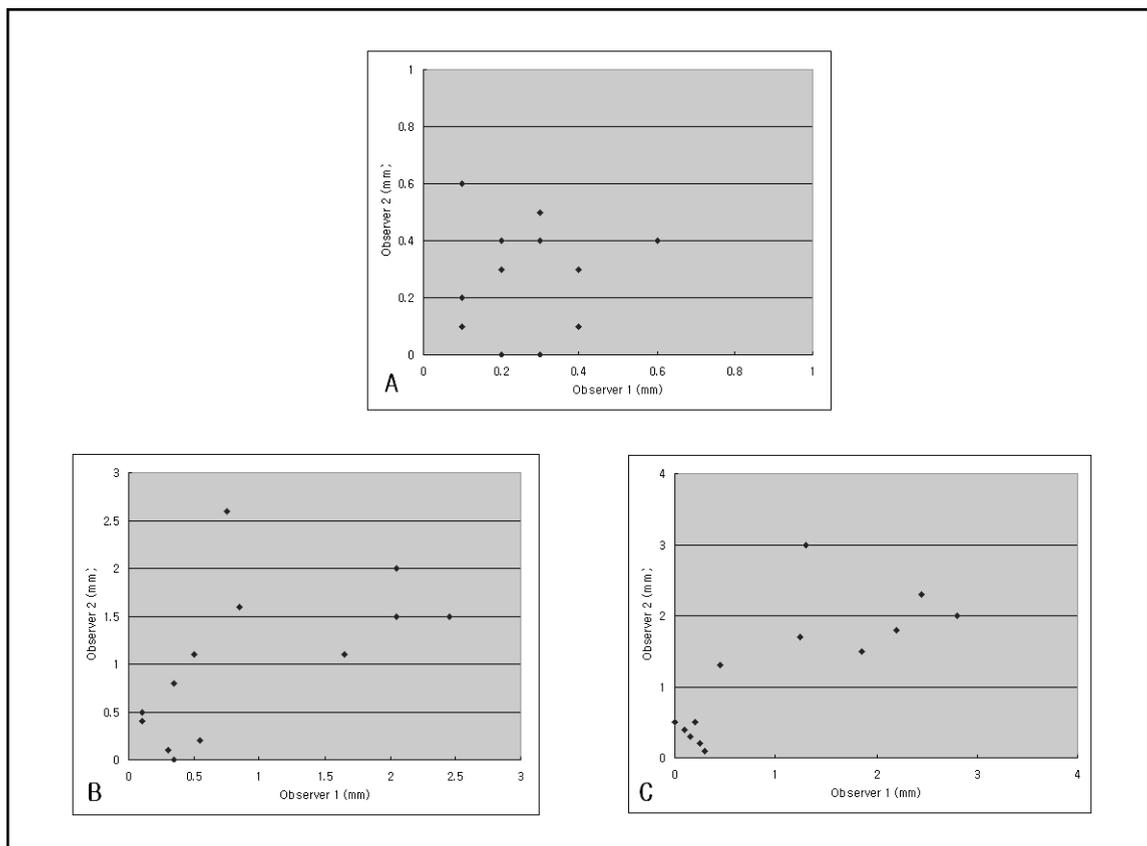


Fig. 4. Comparison of the compliances of skin, subcutis and total tissue by two observers in the forearm. (A) skin, (B) subcutis, (C) total tissue.

RESULTS

Sample Characteristics

Two hundred eight sonographic images were obtained in 13 subjects by two sonographers. The mean body mass (BMI) index of the subjects was 22.40 ± 3.11 . The BMI was not correlated with the thickness or pressure compliance in the soft tissues in the sonographic images.

Comparison of Psychometric and Sonographic Findings

Mean thickness and reliability of the skin and subcutis in the forearm

The mean thicknesses of the skin, subcutis, and total tissues without pressure were 1.39 ± 0.28 mm, 3.55 ± 1.58 mm, and 4.94 ± 1.65 mm, respectively (Table 1). With maximal compression, the mean thicknesses of the skin, subcutis, and total tissues were 1.16 ± 0.19 mm, 2.51 ± 1.05 mm, and 3.67 ± 1.06 mm, respectively. All the intra- and inter-rater correlation coefficients of thickness without pressure in the subcutis and total tissues were >0.75 and accepted as excellent reliability (Table 2). With maximal compression, the coefficients of the subcutis and total tissues were excellent. For skin, the intra-rater reliability without compression was excellent, but the others were fair-to-good.

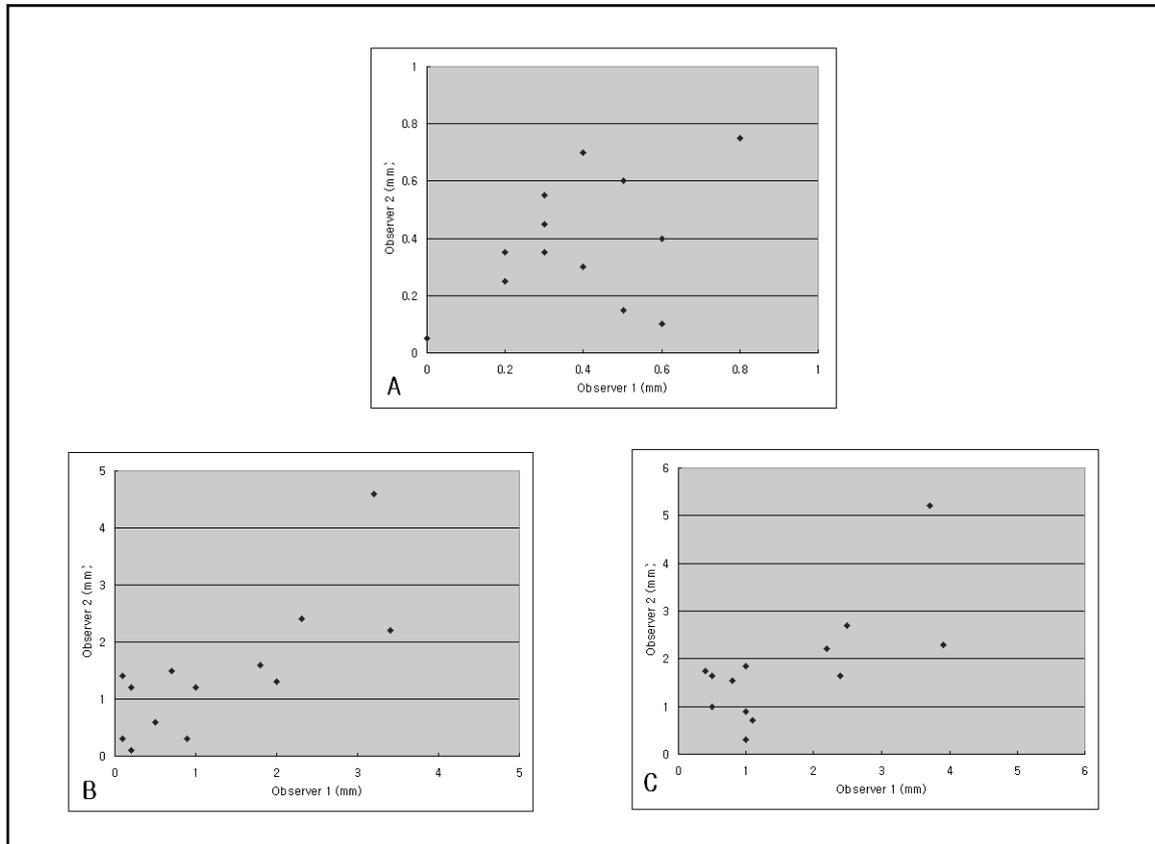


Fig. 5. Comparison of the compliances of skin, subcutis and total tissue by two observers in the upper arm. (A) skin, (B) subcutis, (C) total tissue.

Mean thickness and reliability of the skin and subcutis in the upper arm

The mean thicknesses of the skin, subcutis, and total tissues without pressure were 1.42 ± 0.38 mm, 3.95 ± 1.71 mm, and 5.37 ± 1.78 mm, respectively (Table 1). With maximal compression, the mean thicknesses of the skin, subcutis, and total tissues were 1.02 ± 0.23 mm, 2.47 ± 0.88 mm, and 3.49 ± 0.89 mm, respectively. All the intra- and inter-rater correlation coefficients of thickness without pressure in the subcutis and total tissues were >0.75 and accepted as excellent reliability (Table 3). With maximal compression, the intra-rater coefficients of the subcutis and total tissues were excellent.

However, the inter-rater reliabilities of all tissues were fair-to-good in the upper arm.

Mean compliance of the skin and subcutis. The mean compliances of the skin, subcutis, and total tissues in the forearm were 0.22 ± 0.26 mm, 1.05 ± 0.84 mm, and 1.27 ± 0.97 mm, respectively (Fig. 3 and Fig. 4).

In the upper arm, the mean compliance of the skin, subcutis, and total tissues were 0.40 ± 0.21 mm, 1.49 ± 1.21 mm, and 1.88 ± 1.24 mm, respectively (Fig. 3 and Fig. 5). All the intra-rater correlation coefficients of compliance of the subcutis and total tissues in the forearm and upper arm were >0.75 and accepted as excellent reliability (Table 4). For the inter-rater reliability, only measuring the compliance of the total tissues in the forearm was excellent, but others were fair-to-good.

TABLE 4
ICC of the Soft Tissue Compliance Using Ultrasound

	Forearm		Upper Arm	
	Intra-rater	Inter-rater	Intra-rater	Inter-rate
Skin	0.725**	0.330	0.644**	0.391
Subcutis	0.822**	0.664**	0.887**	0.766**
Total	0.824**	0.806**	0.904**	0.716**

*p<0.05; **p<0.01. Abbreviation: ICC = intraclass correlation coefficient

TABLE 5
ICC of the Soft Tissue Thickness Measurements Using Tape

	Inter-rater	Inter-rater
Forearm	0.983**	0.955**
Upper arm	0.991**	0.975**

*p<0.05; **p<0.01. Abbreviation: ICC = intraclass correlation coefficient

TABLE 6
Correlation Coefficients of Circumference with the Difference of Compliance between Trial 1 and 2 and the Mean of Compliance between Two Observers

		DC in Observer 1	DC in Observer 2	DMC
Forearm	Skin	0.504	0.319	0.009
	Subcutis	0.469	0.301	0.567
	Total	0.536	0.343	0.144
Upper arm	Skin	-0.187	0.143	-0.210
	Subcutis	-0.168	0.261	0.076
	Total	-0.209	0.402	0.008

*p<0.05; **p<0.01. Abbreviation: DC = Difference of compliance between trial 1 and 2; DMC = Difference of mean compliance between two observer.

Circumference measure

The inter- and intra-rater coefficients of the circumference in the forearm and upper arm were >0.75 , and it was a reliable test (Table 5). The difference of compliances between first and second trials or the difference of mean compliances between two sonographers did not show the significant correlation with circumference (Table 6).

DISCUSSION

Lymphedema is defined as a progressive, protein-rich fluid accumulation in the interstitial spaces of the skin that arises as a consequence of impaired lymphatic drainage (1,2). These fluid accumulations can cause irreversible soft tissue fibrosis. The extent of volume change can be affected by soft tissue characteristics. Therefore, the measurement of circumference or volumetric measurements are not sufficient to monitor the progression of lymphedema, and it is necessary to evaluate the soft tissue characteristics. Our ultrasonographic method may reflect the soft tissue characteristics and the status of volume but two points should be authenticated to be used clinically because of inherent disadvantage of ultrasonography (30).

First, the important point is whether the depth of soft tissues can be measured objectively with ultrasonography. Ultrasonography may be a relatively subjective tool, and the measurement parameters may be variable by examiners (30). Our data showed that measuring the depth of soft tissues with ultrasonography could be accepted objectively in the forearm. The surface in front of the upper arm is round, and the reliability of measuring the depth could be low. However, the depth of the subcutis was regular with trials and could be used for evaluation in the soft tissues. Pressure may affect the accuracy of measuring the depth of soft tissues with ultrasonography and our data show that pressure should be controlled for

ultrasonography.

The second issue is whether the change in softness of the skin can be checked with ultrasonography. Tissue tonometry can determine tissue softness and has been used for the outcome of treatment of lymphedema (32,33). Chen et al (34) reported the reliability of measurements for lymphedema in breast cancer patients. The intraclass correlation coefficient of tonometry showed fair-to-good reliability around 0.7, except in the forearm and hand (0.879 and 0.769, respectively). Our results also showed that the reliability of pressure compliance was also excellent in forearm. Comparing tonometry, the inter-rater ICC of pressure compliance with ultrasonography was higher (0.806 vs. 0.714) (34). The reliability of compliance in upper arm was fair-to-good. The thickness was measured with sitting position and supination of arm. Biceps muscles in some subjects were not relaxed, and it may affect the size of subcutis with or without pressure. For evaluation of soft tissue in the upper arm, positional change may be controlled to exclude the factor which can distort the regular value with repeat measurement.

Water displacement and circumference measurement have shown excellent reliability (34). In our study, the reliability of the circumference measurement was excellent. The difference of compliances between first and second trials or the difference of mean compliances between two sonographers did not show a significant correlation with the size of arm. If any correlation was found, the compliance could be changed with various arm size, and it, therefore, might be a significant problem to use our method in a large edematous arm. The fact that the compliance was not related with the size of the arm or BMI may improve potential for clinical use.

For the evaluation of tissue characteristics, Righetti et al (35) and Berry et al (36) adapted poroelastographic techniques with ultrasonography. This technique is a very precise method and evaluates both the

lateral and axial strains of soft tissue. Both poroelastographic technique and our method use “compression” but the meanings are totally different. Poroelastographic technique checks time-dependent mechanical response with compression. However, our method evaluates the change of depth of soft tissue with pressure (compliance). The data from our method may or may not be consistent with those of poroelastographic technique in the same tissue. Compared to the poroelastographic technique, our method can be used simply to monitor the progression of lymphedema in clinical situations.

This study suggests a simple method that can be applied to evaluate the structural changes and softness changes of soft tissues simultaneously in the clinical situation, and that ultrasonography may be a useful tool for measurement of the status of soft tissues. Future studies are needed comparing edematous tissue with serial measurement during treatment of lymphedema.

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