



저작자표시-비영리-동일조건변경허락 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.
- 이차적 저작물을 작성할 수 있습니다.

다음과 같은 조건을 따라야 합니다:



저작자표시. 귀하는 원저작자를 표시하여야 합니다.



비영리. 귀하는 이 저작물을 영리 목적으로 이용할 수 없습니다.



동일조건변경허락. 귀하가 이 저작물을 개작, 변형 또는 가공했을 경우에는, 이 저작물과 동일한 이용허락조건하에서만 배포할 수 있습니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 [이용허락규약\(Legal Code\)](#)을 이해하기 쉽게 요약한 것입니다.

[Disclaimer](#)

의학석사 학위논문

**Correlation among bioimpedance  
analysis, sonographic and  
circumferential measurement in  
assessment of breast cancer-related  
arm lymphedema**

유방암 수술 이후 발생한 림프 부종의 측정방법으로  
바이오 임피던스 측정법과 초음파 측정법, 둘레  
측정법 간의 상관관계

2013년 2월

서울대학교 대학원

의학과 재활의학 전공

최 윤 희

유방암 수술 이후 발생한 림프 부종의  
측정 방법으로 바이오 임피던스  
측정법과 초음파 측정법,  
둘레 측정법 간의 상관관계

지도교수 서 관 식

이 논문을 의학석사 학위논문으로 제출함

2012 년 10 월

서울대학교 대학원

의학과 재활의학 전공

최 윤 희

최윤희의 의학석사 학위논문을 인준함.

2012 년 12 월

위 원 장 \_\_\_\_\_ (인)

부위원장 \_\_\_\_\_ (인)

위 원 \_\_\_\_\_ (인)

**Correlation among bioimpedance  
analysis, sonographic and  
circumferential measurement in  
assessment of breast cancer-related  
arm lymphedema**

by

Yoon-Hee Choi, MD

(Directed by Kwan Sik Seo, MD, PhD)

A Thesis Submitted to the Department of Medicine  
in Partial Fulfillment of the Requirements for the  
Degree of Master of Philosophy in Rehabilitation Medicine at the  
Seoul National University College of Medicine

December 2012

Approved by thesis committee:

Professor \_\_\_\_\_ Chairman

Professor \_\_\_\_\_ Vice Chairman

Professor \_\_\_\_\_

# 학위논문 원문제공 서비스에 대한 동의서

본인의 학위논문에 대하여 서울대학교가 아래와 같이 학위논문 제공하는 것에 동의합니다.

## 1. 동의사항

- ① 본인의 논문을 보존이나 인터넷 등을 통한 온라인 서비스 목적으로 복제할 경우 저작물의 내용을 변경하지 않는 범위 내에서의 복제를 허용합니다.
- ② 본인의 논문을 디지털화하여 인터넷 등 정보통신망을 통한 논문의 일부 또는 전부의 복제, 배포 및 전송 시 무료로 제공하는 것에 동의합니다.

## 2. 개인(저작자)의 의무

본 논문의 저작권을 타인에게 양도하거나 또는 출판을 허락하는 등 동의 내용을 변경하고자 할 때는 소속대학(원)에 공개의 유보 또는 해지를 즉시 통보하겠습니다.

## 3. 서울대학교의 의무

- ① 서울대학교는 본 논문을 외부에 제공할 경우 저작권 보호장치(DRM)를 사용하여야 합니다.
- ② 서울대학교는 본 논문에 대한 공개의 유보나 해지 신청 시 즉시 처리해야 합니다.

**논문 제목 : 유방암 수술 이후 발생한 림프 부종의 측정 방법으로 바이오 임피던스 측정법과 초음파 측정법, 둘레 측정법 간의 상관관계**

학위구분: 석사  · 박사

학 과: 의학과 재활의학 전공

학 번: 2011-21865

연 락 처: 서울대학교 병원 재활의학과

저 작 자: 최 윤 희 (인)

제 출 일: 2013년 2월 4일

서울대학교총장 귀하

## Abstract

# Correlation among bioimpedance analysis, sonographic and circumferential measurement in assessment of breast cancer-related arm lymphedema

Yoon-Hee Choi

Department of Rehabilitation Medicine

The Graduate School

Seoul National University

**Introduction:** New approaches for assessment of lymphedema using bioimpedance analysis and ultrasonography have been introduced recently and both are considered to be reliable and simple. Bioimpedance analysis gives information about extracellular fluid, and ultrasonography provides detailed information about physical properties of the tissue in addition to volume and size. There have been few studies to compare among those

methods and circumferential measurement which is considered as a standard measurement. The aim of the present study was to determine the relationship among bioimpedance analysis, ultrasonography and circumferential measurement.

**Materials and Methods:** Twenty-eight patients with lymphedema after breast cancer surgery underwent bioimpedance analysis, ultrasonography and circumferential measurements. Impedance which reflects the amount of extracellular fluid was measured with 1Hz frequency in affected and unaffected arms. Impedance obtained directly from the device was used to calculate impedance ratios. The ultrasonographic measurement of subcutis thickness at upper arm and forearm was performed with and without compression. The compressibility at affected and unaffected arms was examined by ultrasonography. The circumferences were measured at 10cm proximal and at 10cm distal to the elbow. Using a truncated method, we calculated estimated volumes for upper arm and forearm. We compared circumferential measurements with impedance ratios and sonographic measurements.

**Results:** Impedance ratios measured at upper arm and forearm were strongly correlated with circumferential measurements (interlimb circumferential

difference/ interlimb volume difference calculated as a truncated cone/ interlimb volume ratio; 0.789(p<0.001) and 0.872(p<0.001)/ 0.836(p<0.001) and 0.851(p<0.001)/ 0.802(p<0.001) and 0.841(p<0.001), respectively). Interlimb forearm subcutis thickness differences measured by ultrasonography with and without compression were also highly correlated with circumferential measurements (interlimb circumferential difference/ interlimb volume difference calculated as a truncated cone/ interlimb volume ratio; 0.725(p<0.001) and 0.756(p<0.001)/ 0.798(p<0.001) and 0.826(p<0.001)/ 0.767(p<0.001) and 0.809(p<0.001), respectively). Interlimb upper arm subcutis thickness differences measured by ultrasonography with and without compression were moderately correlated with circumferential measurements. Furthermore, impedance ratios measured at upper arm and forearm were moderately correlated with subcutis thickness with and without compression. However, the interlimb ratio of compressibility measured by ultrasonography showed no or only weak correlation with impedance measurements and circumferential measurements.

**Conclusion:** There was a high degree of concordance among circumferential measurements, bioimpedance analysis and subcutis thickness measured by ultrasonography.

**Keywords:** Lymphedema; Impedance; Ultrasonography

Student number : 2011-21865

# Contents

Abstract.....	i
Contents.....	v
List of Tables.....	vi
List of Figures.....	vii
Introduction.....	1
Materials and Methods.....	4
Results .....	15
Discussion .....	30
Conclusion .....	33
References .....	34
Abstract (Korean) .....	39

## List of Tables

Table 1. Participant characteristics.....	16
Table 2. Circumferential measurements.....	18
Table 3. Ultrasonographic measurements.....	22
Table 4. Correlation between circumferential and bioimpedance measurements.....	24
Table 5. Correlation between circumferential and ultrasonographic measurements.....	27
Table 6. Correlation between bioimpedance and ultrasonographic measurements.....	29

## List of Figures

Fig 1. Sites for measurements.....	6
Fig 2. Multifrequency impedance plethysmograph body composition analyzer... ..	8
Fig 3. Ultrasonographic transducer with pressure sensor.....	11
Fig 4. Reliability of compressibility in subcutis according to the compression force.....	12
Fig 5. Ultrasonographic measurement.....	13

# I. Introduction

Upper limb lymphedema is a clinical manifestation of obstruction or disruption of the lymphatic system as a consequence of breast cancer surgery, radiation therapy or malignancy.(1) The reported incidence of upper limb lymphedema is quite variable from less than 10% to more than 50%, with a prevalence of 13-42% of breast cancer patients.(2-4) In order to document exact incidence and treatment outcomes, reliable, valid and practical measurements and quantifications of upper limb lymphedema are crucial.

There are various diagnostic definitions to diagnose lymphdema such as interlimb circumference difference more than 2 centimeters, interlimb volume difference more than 8 to 10% or 200ml or subjective reports of limb heaviness.(5-7) Conventional measurements include a circumferential measurement such as a tape method and calculated volume which is derived from circumference measures by using the formula for a truncated cone.(8, 9) Due to its convenience and cost-effectiveness, it is most widely used to diagnose lymphedema. Because circumferential measurements assess total limb volume, those are indirect measures and have limitations to detect early changes of lymphedema. Also, reliability issues have been raised.(10, 11)

Total limb volume includes not only the extracellular fluid, which accounts for approximately 25% of total limb volume but also bone, muscle, fat and other soft tissues.(12, 13)

New measurement methods have been introduced to evaluate upper limb lymphedema. Bioimpedance measurements are used to quantify the amount of extracellular fluid directly.(14) Bioimpedance measurements analyze the response of the body to an applied electrical current and estimate body composition.(12) Ultrasonography has been used to evaluate lymphedema for an investigational purpose.(15) Ultrasonographic measurements can analyze physical properties of the tissue and structural alterations in real time.(16) Long standing lymphedema causes a condition known as fibrosis. Also, ultrasonography can measure compressibility, which is one of characteristics and conditions of biomedical tissue in an objective way. As the fluid continually collects in a limb, it becomes hard and less compressible.(17) The compressibility of the skin and subcutis is known to be an important index in order to control the progress of lymphedema.(18)

Although several trials were made to compare different methods, most of them have examined the relationship between circumferential measurements and water displacement or perometry. (19)

The objective of the present study was to determine the relationship among

bioimpedance analysis, ultrasonography and circumferential measurements.

The bioimpedance analysis and ultrasonography were compared with circumferential measurements. In addition, we examined what parameters from those measurements would be more correlated to other measurement methods.

## **II. Materials and Methods**

### **2. 1. Subjects**

The eligible participants were patients 1) with secondary unilateral lymphedema 2) that developed after surgery for breast cancer and 3) which was confirmed by clinical and lymphoscintigraphic examination. For the clinical diagnosis, the circumference of the affected arm measured at forearm and upper arm had to exceed that of the unaffected arm by two or more centimeters. Lymphoscintigraphy evaluated the obstructive pattern of lymphatic drainage in the affected limb and the accumulation of lymphatic fluid. Patients 1) who had primary lymphedema, 2) whose lymphedema was not related with the treatment for breast cancer, and 3) who had bilateral lymphedema were excluded.

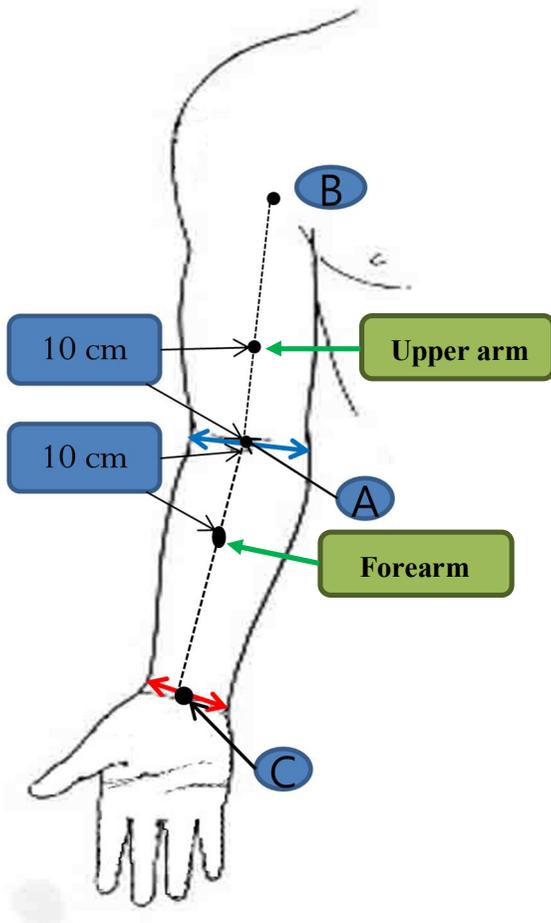
The participants were recruited from the outpatient clinic of Department of Rehabilitation Medicine in Seoul National University Hospital, Seoul, Korea. The study protocol was approved by the institutional review board of our hospital. All study protocol was explained in detail and informed consent was obtained from all the participants.

### **2.2. Measurements of lymphedema**

Lymphedema was measured with bioimpedance analysis, ultrasonography and circumferential measurements.

### **2.2.1. Circumferential measurement**

The circumferences were measured with a measuring tape. Circumferences were measured at upper arm, elbow and forearm on both sides. On the upper arm, the location of measurement was 10 centimeter proximal from the elbow crease along the line between the midpoint of the medial and lateral epicondyles of the humerus and the bicipital groove. On the forearm, the location of measurement was 10cm distal from the elbow crease along the line between the midpoint of the medial and lateral epicondyles and the midpoint of radial and ulnar styloid processes. (Fig. 1)



**Figure 1.** Sites for measurement

(a) Upper arm: In the line from the midpoint of the medial and lateral epicondyle(A) to the bicipital groove(B), 10cm proximal from (A)

(b) Forearm: In the line from the midpoint of the medial and lateral epicondyle(A) to the midpoint of radial and ulnar styloid processes(C), 10cm distal from (A)

One experienced doctor measured circumferences. The volumes of forearm and upper arm were derived from circumference measures by using the formula for a truncated cone;  $V = h (C_1^2 + C_1C_2 + C_2^2) / 12$  [1]; V=volume; h=height of the segment; C1 and C2=circumference at each end of the segment.

The interlimb circumference difference, interlimb volume difference and interlimb volume ratio were used for an analysis.

### **2.2.2. Bioimpedance measurement**

A multifrequency impedance plethysmograph body composition analyzer (InBodyS10, Biospace, Seoul, Korea) (Fig. 2) was used to measure extracellular fluid volume.



**Figure 2.** Multifrequency impedance plethysmograph body composition analyzer

It takes readings from the body using an eight-point tactile electrode method. During impedance measurements, all participants were lying on the back at the bed. Previous literatures showed that the best frequency to detect extracellular fluid is 0 kHz (or DC). However, measurement at this frequency is not possible in practice due to the high skin impedance at DC, and an estimate is usually determined from low frequency measurements. Impedance measured with 1Hz frequency in affected and unaffected arms was used for analysis in this study. Impedances obtained directly from the device were used to calculate impedance ratios. Because impedance decreases with increased fluid, the ratio was expressed as impedance on unaffected limb/impedance on affected limb to provide a lymphedema index greater than 1.

### **2.2.3. Ultrasonographic measurement**

The subjects were placed supine on an examination table with the forearm supinated and relaxed. An ultrasound unit (Accuvix V10EX-DOM-00, Medison Co., Seoul, Korea) evaluated the soft tissue on the upper arm and forearm with a 7.5MHz linear-array transducer. Ultrasonographic measurements were performed at the same points with circumferential measurements for upper arms and forearms on both affected and unaffected sides.

Imaging of the skin, subcutis, muscle, and sometimes bone was possible. Ultrasound gel was applied liberally to the skin and the probe placed transversely on the arm. To measure the thickness of the skin and subcutis, an ultrasonographer applied negligible pressure by pasting a sufficient amount of lubricant so that the contour of the tissue beneath a transducer was not distorted.

Also, the ultrasonographic measurements of skin and subcutis thickness at upper arm and forearm in affected and unaffected sides were performed with control of precise pressure. A portable pressure sensor (HF-1, Japan Instrumentation System Co., Yokohama, Japan) was attached to the probe and the examiner controlled pressure as 2N by monitoring the sensor. (Fig. 3)

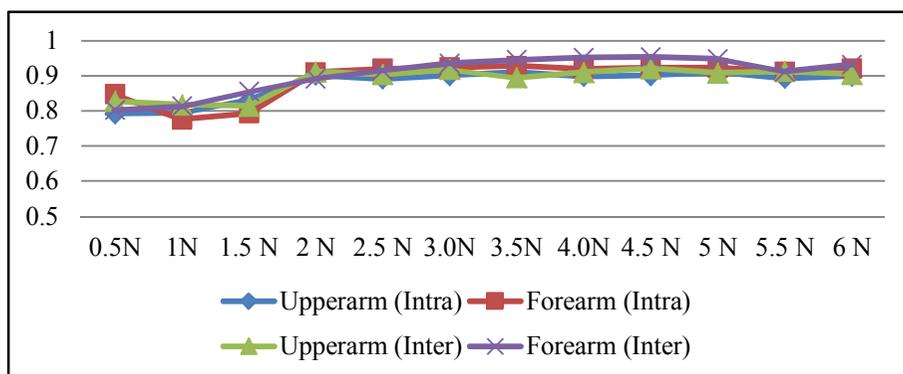


**Figure 3.** Ultrasonographic transducer with pressure sensor.

A portable pressure sensor was attached to the probe and the examiner controlled pressure as 2N by monitoring the sensor.

The previous study showed at least 2N needs for achieving a high reliability.

(Fig. 4)(20)

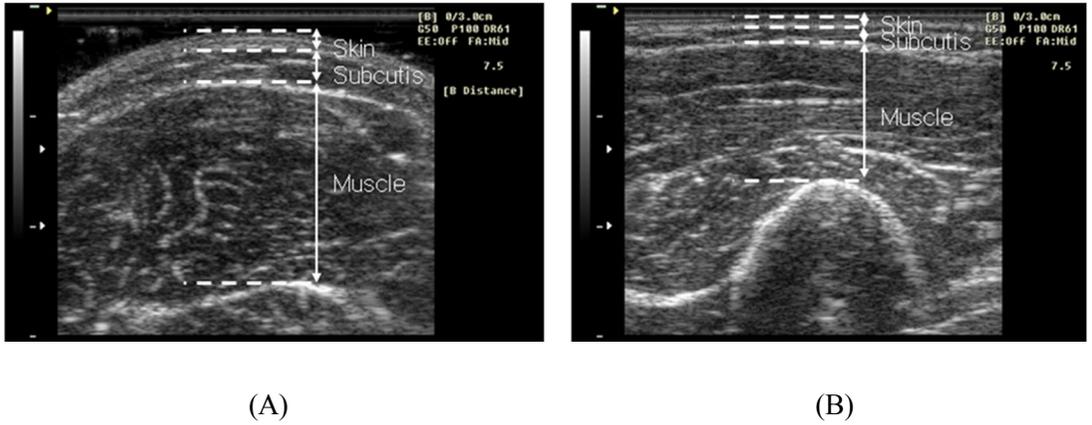


N	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6
U (Intra)	0.792	0.795	0.832	0.902	0.891	0.901	0.91	0.898	0.901	0.91	0.893	0.899
F (Intra)	0.848	0.776	0.793	0.91	0.92	0.924	0.928	0.92	0.924	0.923	0.912	0.921
U (Inter)	0.828	0.818	0.814	0.912	0.904	0.918	0.895	0.91	0.921	0.908	0.913	0.905
F (Inter)	0.802	0.813	0.855	0.892	0.916	0.936	0.946	0.952	0.954	0.948	0.912	0.932

**Figure 4.** Reliability of compressibility in subcutis according to the compression force.

Intra-rater and Inter-rater reliability were very good when measured with pressure above 2.0 N. Intra, intra-rater reliability; Inter, inter-rater reliability; U, upper arm; F, forearm.

Skin thickness was defined as distance between the bottom of the entry-echo and the skin-subcutis boundary. Subcutis thickness was measured between the skin-subcutis boundary and the subcutis-muscle boundary (Fig. 5).



**Figure 5.** Ultrasonographic measurements with negligible pressure (A) and with control of precise pressure (B)

On the images captured on the upper arm and forearm, the thickness of skin and subcutis were measured by using console measurement tools on the ultrasound unit.

The compressibility was calculated as follows.

$$\frac{\text{thickness measured without pressure} - \text{thickness measured with precise pressure}}{\text{thickness measured without pressure}}$$

#### **2.2.4 Characteristics of participants**

The demographic and clinical variables of the patients were described. The demographic variables included the age at study enrollment and the body mass index (BMI). The clinical variables were included the side of the dominant hand, type of surgery, the time after surgery, a history of lymph node dissection, radiation therapy and chemotherapy, the tumor stage and the duration of lymphedema.

### **2.3. Data Analysis**

The SPSS 18.0 program for Windows was used for the statistical analysis with a value of  $p < 0.05$  considered significant. We compared circumferential measurements with sonographic and impedance ratios by Pearson's correlation analysis. Comparison of compressibility between affected and

unaffected side was performed by Student's *t*-test.

### **III. Results**

#### **3. 1. Subjects**

Baseline characteristics of participants are summarized in Table 1. Twenty-eight women, ages 30 to 77 years (mean age  $54.8 \pm 9.7$  years, SD) were enrolled. All patients had operation. Twelve (42.9%) underwent quadrantectomy, 6 (21.4%) underwent breast conserving surgery and 6 (21.4%) underwent modified radical mastectomy. Axillary lymph node dissection was performed in 21 patients (75.5%). 25 patients (89.3%) received chemotherapy and 24 patients (86.7%) got radiotherapy. Eighteen patients (64.3%) affected in right side and 10 (35.7%) affected in left side. Lymphangiography was performed in 20 patients (71.14%). It showed definite obstruction in 7 (25%), suspicious obstruction in 11 (39.3%) and no definite obstruction in 2 (7.1%).

**Table 1. Participant characteristics**

Characteristic	
Age (year)	54.82±9.73
BMI (Kg/m <sup>2</sup> )	24.29±3.09
Affected limb	18R:10L
Surgery	
Quadrantectomy	12 (42.9%)
Breast conserving surgery	6 (21.4%)
Modified radical mastectomy	6 (21.4%)
Others	4 (14.3%)
Axillary lymph node dissection	
Yes	21 (75.0%)
No	2 (7.1%)
N/A	5 (17.9%)
Chemotherapy	25 (89.3%)
Radiotherapy	24 (85.7%)
Time since surgery (months)	57.21±53.20
Time since onset of lymphedema (months)	30.36±26.73

### **3.2. Circumferential measurement (Table 2)**

The mean circumferential difference at distal 10cm and at proximal 10cm from the elbow crease was  $2.72\pm 2.68$  and  $2.84\pm 2.23$ , respectively.

The mean interlimb volume difference at forearm and at upper arm was  $0.11\pm 0.12\text{cm}^3$  and  $0.12\pm 0.12\text{cm}^3$ , respectively.

The mean interlimb ratio at forearm and at upper arm was  $1.24\pm 0.26$  and  $1.22\pm 0.21$ , respectively.

**Table 2. Circumferential measurements**

	Affected (mean±SD)	Unaffected (mean±SD)	Interlimb difference	Ratio (mean±SD)
Circumference at the MCP (cm)	19.01±0.90	18.88±1.38	0.13±1.23	
Circumference at the wrist (cm)	17.34±1.53	16.30±0.99	1.04±1.28	
Circumference at forearm (cm)	25.51±3.19	22.79±1.60	2.72±2.68	
Circumference at the elbow (cm)	27.36±3.43	24.80±1.73	2.56±2.71	
Circumference at upper arm (cm)	31.10±3.38	28.26±2.60	2.84±2.23	
Volume at forearm (cm <sup>3</sup> )	0.56±0.15	0.45±0.06	0.11±0.12	1.24±0.26
Volume at upper arm (cm <sup>3</sup> )	0.69±9.16	0.56±0.09	0.12±0.12	1.22±0.21

### **3.3. Bioimpedance measurement**

The mean values of impedance for affected side and unaffected side were  $331.62 \pm 79.60$  and  $402.59 \pm 44.90$ , respectively.

The mean value for the interlimb ratio of impedance (unaffected side/affected side) was  $1.27 \pm 0.31$ .

### **3.4. Ultrasonographic measurement (Table 3)**

#### **3.4.1 Upper arm**

##### **3.4.1.1 Measurement with negligible pressure and with control of precise pressure**

Skin thickness measured with negligible pressure at affected and unaffected side was  $0.19 \pm 0.08$  and  $0.16 \pm 0.03$ , respectively. Subcutis thickness measured with negligible pressure at affected and unaffected side was  $0.91 \pm 0.41$  and  $0.72 \pm 0.20$ , respectively. Interlimb subcutis thickness was  $0.19 \pm 0.42$ .

Skin thickness measured with control of precise pressure at affected and unaffected side was  $0.15 \pm 0.05$  and  $0.13 \pm 0.02$ , respectively. Subcutis thickness measured with control of precise pressure at affected and unaffected side was  $0.58 \pm 0.27$  and  $0.43 \pm 0.11$ , respectively. Interlimb subcutis thickness was  $0.16 \pm 0.28$ .

### **3.4.1.2 Compressibility**

The compressibility of skin and subcutis measured at an affected upper arm was  $-0.02 \pm 1.23$  and  $0.34 \pm 0.15$ . The compressibility of skin and subcutis measured at a unaffected upper arm was  $0.19 \pm 0.14$  and  $0.39 \pm 0.13$ .

There was no difference in the compressibility of skin and subcutis between affected and unaffected side.

### **3.4.2 Forearm**

#### **3.4.2.1 Measurement with negligible pressure and with control of precise pressure**

Skin thickness measured with negligible pressure at affected and unaffected side was  $0.65 \pm 0.55$  and  $0.18 \pm 0.05$ , respectively. Subcutis thickness measured with negligible pressure at affected and unaffected side was  $1.24 \pm 0.90$  and  $0.77 \pm 0.31$ , respectively. Interlimb subcutis thickness was  $0.47 \pm 0.91$ .

Skin thickness measured with control of precise pressure at affected and unaffected side was  $0.15 \pm 0.06$  and  $0.13 \pm 0.03$ , respectively. Subcutis thickness measured with control of precise pressure at affected and unaffected side was  $0.86 \pm 0.78$  and  $0.46 \pm 0.23$ , respectively. Interlimb subcutis thickness was  $0.16 \pm 0.28$ .

### **3.4.2.2 Compressibility**

The compressibility of skin and subcutis measured at an affected forearm was  $0.51 \pm 0.37$  and  $0.35 \pm 0.16$ . The compressibility of skin and subcutis measured at a unaffected forearm was  $0.25 \pm 0.19$  and  $0.38 \pm 0.21$ .

There is no difference in the compressibility of skin and subcutis between affected and unaffected side.

**Table 3. Ultrasonographic measurements**

	Subcutis thickness without pressure		Subcutis thickness with pressure	
	Affected	Unaffected	Affected	Unaffected
Forearm	1.24±0.90	0.77±0.31	0.86±0.78	0.46±0.23
Upper arm	0.91±0.41	0.72±0.20	0.58±0.27	0.43±0.11
	Skin thickness without pressure		Skin thickness with pressure	
	Affected	Unaffected	Affected	Unaffected
Forearm	0.65±0.55	0.18±0.05	0.15±0.06	0.13±0.03
Upper arm	0.19±0.08	0.16±0.03	0.15±0.05	0.13±0.02
	Subcutis Compressibility at affected limb		Subcutis Compressibility at unaffected limb	
Forearm	0.35±0.16		0.38±0.21	
Upper arm	0.34±0.15		0.39±0.13	

### **3.5. Relationship among measurement methods.**

#### **3.5.1. Correlation between circumferential and bioimpedance measurements (Table 4)**

Impedance ratios measured at upper arm and forearm were highly correlated with circumferential difference (0.789( $p < 0.001$ ) and 0.872( $p < 0.001$ ), respectively) and interlimb volume difference calculated as a truncated cone (0.836( $p < 0.001$ ) and 0.851( $p < 0.001$ ), respectively). Impedance ratios measured at upper arm and forearm were highly correlated with interlimb volume ratio (0.802( $p < 0.001$ ) and 0.841( $p < 0.001$ ), respectively).

**Table 4. Correlation between circumferential and bioimpedance measurements**

	Upper arm		Forearm	
	<i>r</i>	<i>p-value</i>	<i>r</i>	<i>p-value</i>
Impedance ratio vs				
Interlimb circumference difference	0.789	<0.001	0.872	<0.001
Interlimb volume difference	0.836	<0.001	0.851	<0.001
Interlimb volume ratio	0.802	<0.001	0.841	<0.001

*r*: Pearson's correlation coefficient

## **3.5.2. Correlation between circumferential and ultrasonographic measurements (Table 5)**

### **3.5.2.1. Upper arm**

The interlimb subcutis thickness differences measured with and without pressure were correlated with interlimb circumferential difference (0.541 (p=0.003) and 0.598(p=0.001), respectively), with interlimb volume difference (0.516(p=0.005) and 0.597(p=0.001), respectively) and with interlimb volume ratio (0.452(p=0.016) and 0.527(p=0.004), respectively).

The interlimb ratio of compressibility was not correlated with interlimb circumferential difference (0.236(p=0.226)), with interlimb volume difference (0.165(p=0.400)) and with interlimb volume ratio (0.178(p=0.364)).

### **3.5.2.2 Forearm**

The interlimb subcutis thickness differences measured with and without pressure were correlated with interlimb circumferential difference (0.756(p<0.001) and 0.725(p<0.001), respectively), with interlimb volume difference (0.826(p<0.001) and 0.798(p<0.001), respectively) and with interlimb volume ratio (0.809(p<0.001) and 0.767(p<0.001), respectively).

The interlimb ratio of compressibility was weakly correlated with interlimb circumferential difference (0.393(p=0.039)), with interlimb volume difference

(0.346( $p=0.072$ )) and with interlimb volume ratio (0.391( $p=0.040$ )).

**Table 5. Correlation between circumferential and ultrasonographic measurements**

	<i>r</i> ( <i>p</i> -value)	
	Forearm	Upper arm
Interlimb subcutis thickness difference without pressure vs		
Interlimb circumference difference	0.725(<0.001)	0.598 (0.001)
Interlimb volume difference	0.798 (<0.001)	0.597 (0.001)
Interlimb volume ratio	0.767 (<0.001)	0.527 (0.004)
Interlimb subcutis thickness difference with pressure vs		
Interlimb circumference difference	0.756 (<0.001)	0.541 (0.003)
Interlimb volume difference	0.826 (<0.001)	0.516 (0.005)
Interlimb volume ratio	0.809 (<0.001)	0.452 (0.016)
Interlimb ratio of compressibility vs		
Interlimb circumference difference	0.393 (0.039)	0.236 (0.226)
Interlimb volume difference	0.346 (0.072)	0.165 (0.400)
Interlimb volume ratio	0.391 (0.040)	0.178 (0.364)

*r*: Pearson's correlation coefficient

### **3.5.3. Correlation between bioimpedance and ultrasonographic measurements (Table 6)**

Impedance ratios measured at upper arm were correlated with interlimb subcutis thickness difference with and without pressure (0.504( $p=0.006$ ) and 0.623( $p<0.001$ ), respectively) and those measured at forearm (0.561( $p=0.002$ ) and 0.555( $p=0.002$ ), respectively). However, the interlimb ratios of compressibility at upper arm and forearm were not correlated with impedance ratio (0.255( $p=0.190$ ) and 0.228( $p=0.244$ ), respectively).

**Table 6. Correlation between bioimpedance and ultrasonographic measurements**

	Upper arm		Forearm	
	<i>r</i>	<i>p-value</i>	<i>r</i>	<i>p-value</i>
Interlimb subcutis thickness difference without pressure	0.623	<0.001	0.555	0.002
Interlimb subcutis thickness difference with pressure	0.504	0.006	0.561	0.002
Interlimb ratio of compressibility	0.228	0.244	0.255	0.190

*r*: Pearson's correlation coefficient

## IV. Discussion

We found that there is a strong agreement of circumferential measures with impedance ratios at upper arm and forearm and circumferential measures with interlimb subcutis thickness difference at forearm measured by ultrasonography but only a moderate agreement of impedance ratios with interlimb subcutis thickness difference at upper arm and forearm and circumferential measures with interlimb subcutis thickness difference at upper arm.

Documenting differences in limb size and determining quantitative discrepancies between patients' unaffected and affected limbs is critical in the evaluation of lymphedema. Assessment of lymphedema is most commonly based on abnormal limb size determined from circumferential measurements of the limb. Irrespective of how limb size is determined, circumference and volume are affected by tissues that may change independently from lymphedema, such as muscle and fat.(21) Size differences from left-right dominance, muscle atrophy, fibrous tissue deposition, or weight gain may be inaccurately attributed to fluid accumulation.(22) In addition, it requires the significant amount of time necessary to perform the measurements and the

high potential for measuring error.(14)

Bioimpedance analysis is a convenient and quick method and has proven to be useful in discerning limb size and fluid accumulation differences in patients with lymphedema.(12, 13, 23-25) Although bioimpedance analysis can accurately measure extracellular accumulation of lymphatic fluid because low frequency currents selectively pass through extracellular fluid compartments, it cannot quantify the other tissue elements that increase aside from the interstitial fluid, such as fibrous and adipose tissue deposition. (14) In addition, the exact reference value for impedance ratios is not well established and impedance ratio in a patient with bilateral lymphedema can be anticipated as normal.(26)

Ultrasonography can safely and simply assess structural alterations and the severity of lymphedema. Ultrasonography is easily accessible in a clinic and can visualize architecture in real time. The results from the present study demonstrated that an increase of circumference and calculated volume in an affected limb was agreed to an increase of subcutis thickness measured by ultrasonography. However, skin thickening was minimal in lymphedematous limb. We anticipated that severe lymphedematous limb would be more fibrotic and less compressible. We evaluated the compressibility by a dynamic method with pressure. The compressibility failed to show a strong correlation

with the severity measured by circumferential and bioimpedance measurements. We have limitations to evaluate the compressibility by applying pressure with an ultrasound probe and calculating the deformation of the tissue using the ultrasound image. The way we conducted could assess only the stress and the strain at the tissue surface, so it was impossible to discriminate whether estimated value indicated the superficial part or the deep part. For example, if the shallow part is fibrotic, the deep part would be estimated to be less soft than it really is. Fukuda et al. suggested soft tissue model composing three-layered structure. The skin, subcutis and muscle compose a layered structure and the lymphatic fluid remains in the subcutaneous tissue layer in a patient with lymphedema. (18) Every layer has its own compressibility and three layers have three different compressibilities. Even though we estimated subcutis compressibility separately, compressibility of other tissues could affect the measured value to each other. To quantify compressibility and fibrosis, new assessment methods need to be developed.

In addition, only few patients who had fibrotic change in lymphedematous arm could be included in the present study. Large number of patients who have a wide range of elasticity will be required to evaluate the compressibility in future studies.

## V. Conclusion

There was a high degree of concordance among circumferential measurements, the impedance ratios as determined by the bioimpedance analysis and subcutis thickness measured by ultrasonography.

Impedance ratios measured at upper arm and forearm were highly correlated with interlimb circumferential difference, interlimb volume difference and interlimb volume ratio. Impedance ratios measured at upper arm and forearm were correlated with subcutis thickness on affected side measured by ultrasonography. Also, subcutis thickness at affected side measured by ultrasonography was correlated with interlimb circumferential difference, interlimb volume difference and interlimb volume ratio. Impedance measurements and ultrasonographic measurements not only provide accurate information about the size as circumferential measurements but they also have different advantages to evaluate the patient with upper limb lymphedema. To choose an appropriate method in a clinical setting, the aim of the evaluation, availability and cost should be considered.

## VI. Reference

1. Murdaca G, Cagnati P, Gulli R, Spano F, Puppo F, Campisi C, et al. Current views on diagnostic approach and treatment of lymphedema. *The American journal of medicine*. 2012;125(2):134-40.
2. Petrek JA, Heelan MC. Incidence of breast carcinoma-related lymphedema. *Cancer*. 1998;83(12 Suppl American):2776-81.
3. Ridings P, Bucknall TE. Modern trends in breast cancer therapy: towards less lymphoedema? *European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology*. 1998;24(1):21-2.
4. Deo SV, Ray S, Rath GK, Shukla NK, Kar M, Asthana S, et al. Prevalence and risk factors for development of lymphedema following breast cancer treatment. *Indian journal of cancer*. 2004;41(1):8-12.
5. Stout Gergich NL, Pfalzer LA, McGarvey C, Springer B, Gerber LH, Soballe P. Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. *Cancer*. 2008;112(12):2809-19.
6. Armer JM. The problem of post-breast cancer lymphedema: impact and measurement issues. *Cancer Invest*. 2005;23(1):76-83.
7. Hayes S, Cornish B, Newman B. Comparison of methods to

diagnose lymphoedema among breast cancer survivors: 6-month follow-up.

Breast Cancer Res Treat. 2005;89(3):221-6.

8. Tewari N, Gill PG, Bochner MA, Kollias J. Comparison of volume displacement versus circumferential arm measurements for lymphoedema: implications for the SNAC trial. ANZ journal of surgery. 2008;78(10):889-93.

9. Deltombe T, Jamart J, Recloux S, Legrand C, Vandebroeck N, Theys S, et al. Reliability and limits of agreement of circumferential, water displacement, and optoelectronic volumetry in the measurement of upper limb lymphedema. Lymphology. 2007;40(1):26-34.

10. Gerber LH. A review of measures of lymphedema. Cancer. 1998;83(12 Suppl American):2803-4.

11. Sander AP, Hajer NM, Hemenway K, Miller AC. Upper-extremity volume measurements in women with lymphedema: a comparison of measurements obtained via water displacement with geometrically determined volume. Physical therapy. 2002;82(12):1201-12.

12. Cornish B. Bioimpedance analysis: scientific background. Lymphat Res Biol. 2006;4(1):47-50.

13. Cornish BH, Bunce IH, Ward LC, Jones LC, Thomas BJ. Bioelectrical impedance for monitoring the efficacy of lymphoedema treatment programmes. Breast Cancer Res Treat. 1996;38(2):169-76.

14. Warren AG, Janz BA, Slavin SA, Borud LJ. The use of bioimpedance analysis to evaluate lymphedema. *Ann Plast Surg.* 2007;58(5):541-3.
15. Han Nm, Cho Yj, Hwang Js, Kim Hd, Cho Gy. Usefulness of Ultrasound Examination in Evaluation of Breast Cancer-Related Lymphedema. *J Korean Acad Rehabil Med.* 2011;35(1):101-9.
16. Saijo Y. High resolution biomedical imaging-multimodal ultrasound microscope and combination with optics. *J Acoust Soc Am.* 2012;131(4):3495.
17. De Cock HE, Affolter VK, Wisner ER, Ferraro GL, MacLachlan NJ. Progressive swelling, hyperkeratosis, and fibrosis of distal limbs in Clydesdales, Shires, and Belgian draft horses, suggestive of primary lymphedema. *Lymphat Res Biol.* 2003;1(3):191-9.
18. Fukuda O, Tsubai M, Ueno N. Impedance estimation of soft tissue using ultrasound signal. *Conf Proc IEEE Eng Med Biol Soc.* 2007;2007:3563-8.
19. Jain MS, Danoff JV, Paul SM. Correlation between bioelectrical spectroscopy and perometry in assessment of upper extremity swelling. *Lymphology.* 2010;43(2):85-94.
20. Hwang BK, Lee DH, Park JE, Lee KJ, Kim SK, Seo KS, editors. Optimal Pressure Measurements of Lymphedema with Ultrasonography in

Postoperative Breast Cancer Patients. Proceedings of the 13th International Congress on Clinical Ultrasound of the Spanish Society of General Medicine; 2012 Apr 22-24; Madrid, Spain.

21. Czerniec SA, Ward LC, Refshauge KM, Beith J, Lee MJ, York S, et al. Assessment of breast cancer-related arm lymphedema--comparison of physical measurement methods and self-report. *Cancer Invest.* 2010;28(1):54-62.
22. Mikes DM, Cha BA, Dym CL, Baumgaertner J, Hartzog AG, Tacey AD, et al. Bioelectrical impedance analysis revisited. *Lymphology.* 1999;32(4):157-65.
23. Cornish BH, Chapman M, Hirst C, Mirolo B, Bunce IH, Ward LC, et al. Early diagnosis of lymphedema using multiple frequency bioimpedance. *Lymphology.* 2001;34(1):2-11.
24. Cornish BH, Ward LC, Thomas BJ, Bunce IH. Quantification of lymphoedema using multi-frequency bioimpedance. *Appl Radiat Isot.* 1998;49(5-6):651-2.
25. Ward L, Winall A, Isenring E, Hills A, Czerniec S, Dylke E, et al. Assessment of bilateral limb lymphedema by bioelectrical impedance spectroscopy. *Int J Gynecol Cancer.* 2011;21(2):409-18.
26. Ward LC, Dylke E, Czerniec S, Isenring E, Kilbreath SL.

Confirmation of the reference impedance ratios used for assessment of breast cancer-related lymphedema by bioelectrical impedance spectroscopy. *Lymphat Res Biol.* 2011;9(1):47-51.

## 초 록

**서론:** 최근 림프부종을 평가하기 위한 방법으로 바이오 임피던스 측정법과 초음파 측정법이 소개되고 있고, 이전 연구 결과에 따르면 둘다 신뢰도가 높고, 간단하다고 알려져 있다. 바이오 임피던스 측정법은 세포외 용액에 대한 정보를 제공하고, 초음파는 부피나 크기 증가뿐 아니라 조직의 물리적 특성에 대한 자세한 정보도 제공한다. 현재까지 바이오 임피던스 측정법과 초음파 측정법을 기존의 측정법인 둘레측정법과 비교하는 연구가 거의 이루어지지 않았다. 이번 연구의 목표는 둘레 측정법에 대한 바이오 임피던스, 초음파 측정법 간의 상관 관계를 평가하는 것이었다.

**방법:** 총 28명의 유방암 수술 후 발생한 림프부종 환자들을 대상으로 둘레 측정법, 바이오 임피던스, 초음파 측정법을 이용하여 평가하였다. 임피던스는 세포외액의 양을 평가하는 방법으로 이환된 팔과 건측 팔 모두에서 1Hz 주파수를 이용하여 측정하였다. 기계에서 측정된 임피던스 값을 이환측과 건측의 비를 구하여 분석에 이용하였다. 초음파 측정법은 상완 및 전완에서 압력을 주지 않고, 또 특정 압력을 가하여 얻어진 초음파 이미지에서 피부와 피하조직의 두께를 측정하였다. 둘레측정법으로는 팔꿈치에서

10cm 근위와 10cm 원위에서 테이프를 이용하여 둘레를 측정하고, 여기에서 얻어진 둘레를 원뿔 공식에 대입하여 추정된 부피를 계산하였다. 둘레 측정법과 바이오 임피던스, 초음파 측정법을 비교하여 각각의 상관 관계를 평가하였다.

**결과:** 이환측과 건측의 임피던스 비는 측정된 이환측과 건측의 둘레의 차이와 강한 상관 관계(각각 0.789( $p < 0.001$ ) 과 0.872( $p < 0.001$ ))를 보이며 이환측과 건측의 부피 차이(각각 0.836( $p < 0.001$ )과 0.851( $p < 0.001$ )), 이환측과 건측의 부피 비(각각 0.802( $p < 0.001$ )과 0.841( $p < 0.001$ ))와도 강한 상관 관계를 보였다. 초음파로 전완에서 압력을 가하면서와 가하지 않으면서 측정한 피하 조직의 이환측과 건측의 두께 차이는 둘레의 차이(각각 0.725( $p < 0.001$ )과 0.756( $p < 0.001$ ))와 부피의 차이(각각 0.798( $p < 0.001$ ) 과 0.826( $p < 0.001$ )), 부피의 비(각각 0.767( $p < 0.001$ )과 0.809( $p < 0.001$ ))와도 높은 상관 관계를 가졌다. 또한, 초음파로 상완에서 측정한 피하 조직의 두께 차이는 둘레 측정법에 의해 측정 및 계산된 값과 중증도의 상관관계를 보였다. 임피던스의 비는 상완 및 전완에서 측정한 피하 조직의 두께와 중증도의 상관 관계를 보였다. 그러나 초음파로 측정된 이환측과 건측의 압축률의 비는 둘레 측정법과 바이오 임피던스

측정법으로 측정된 값과 의미있는 상관관계를 보이지는 않았다.

**결론:** 바이오 임피던스 측정법으로 측정한 이환측과 건측의 임피던스 비와 초음파로 측정한 이환측과 건측의 피하 조직의 두께 차이, 둘레 측정법으로 측정한 둘레와 계산된 부피는 서로 강한 상관 관계를 가졌다.

**주요어:** 림프부종; 임피던스; 초음파

**학번:** 2011-21865