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EVALUATION OF LEG EDEMA USING A MULTIFREQUENCY IMPEDANCE METER IN PATIENTS WITH LYMPHATIC OBSTRUCTION

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ABSTRACT

To evaluate quantitatively local edema, electrical tissue impedance in the leg was measured with a multifrequency impedance meter in 10 patients without edema and in 10 other patients with lymphedema after hysterectomy for uterine cervical cancer (Groups 1 and 2, respectively). Equivalent resistivity of extra- and intracellular fluid (RE, RI, respectively) and the ratio RI/RE were calculated. The difference in mean RE between Groups 1 and 2 was significant ($p < 0.05$). In four patients in Group 1 and nine in Group 2, simultaneous measurements were carried out on both legs. The differences between mean RE and RI/RE in Group 2 were significant ($p < 0.05$, $p < 0.025$, respectively). In these 13 patients, correlation coefficients between the ratio of cross-sectional areas of both legs, and both RE and RI/RE were -0.614 ($p < 0.05$) and 0.805 ($p < 0.001$), respectively. The results suggest that RE and RI/RE could be used as sensitive indicators of local edema.

A method to measure local edema in clinical practice and for research is urgently needed. Watanabe et al. (1,2) have previously reported on the application of electrical impedance (Zo) to the legs, using a Minnesota impedance cardiograph, to evaluate the degree of edema. Although Zo is a useful index for this purpose, it has limitations; specifically, whereas Zo correlates roughly with the change of fluid volume in the leg between the electrodes, it cannot delineate the distribution of tissue water between the extra- and intracellular spaces.

An apparatus capable of measuring the resistance of extra- and intracellular fluid (Re, Ri) by referring to the frequency characteristics of living tissues was developed by Haeno et al. (3). They showed that equivalent resistivity of extracellular fluid (RE) increased with the decrease in body weight after hemodialysis (3). The purpose of the present paper is to report on the results obtained using this apparatus in patients with chronic peripheral lymphedema after radical hysterectomy for uterine cervical cancer. The usefulness and the limitations of this method in demonstrating the distribution of water in edematous tissues is also analyzed.

MATERIALS AND METHODS

Twenty patients were examined after undergoing hysterectomy for uterine cervical cancer with radical pelvic lymphadenectomy. The patients were divided into two groups; Group 1 consisted of 10 patients without leg edema and Group 2 of 10 other patients with definite edema in at least one leg (*Tables 1,2*) (4). Two patients of Group 2 exhibited a moderate degree of edema also in the other leg (patients #11,12). In all patients in Group 2, edema was present for at least three

Table 1
Measurements of Equivalent Resistivities of Extra- and Intracellular Fluid in the Legs of Postoperative Patients Without Leg Edema (Group 1) Using a Multifrequency Impedance Meter

Patient No.	Age (years)	Height (cm)	Weight (kg)	Side Examined	Circum-ference (cm)	RE (Ω.cm)	RI (Ω.cm)	Cm (nF/cm)	RI/RE
1	55	155	52	r	29.8	226	722	3.9	3.2
2	63	145.5	46.5	r	32.5	229	1040	2.8	4.5
3	67	152.5	43.5	r	27.9	211	735	3.1	3.5
4	43	160	73	r	35.9	289	869	3.1	3.0
5	62	150	46	r	30.9	266	648	4.7	2.4
6	44	157	51.5	r	34.0	223	713	3.3	3.2
7	49	150	36	r	25.9	230	797	3.0	3.5
8	62	157	61	r	33.8	267	1200	2.1	4.5
9	44	160	65	r	35.5	296	674	4.7	2.3
10	49	153	57	r	32.6	348	603	4.3	1.7
Mean	53.8	154.0	53.2		31.9	259	800	3.5	3.2
± SD	9.1	4.7	11.0		3.3	43	188	0.9	0.9
(n=10)									

RE: equivalent resistivity of extracellular fluid; RI: equivalent resistivity of intracellular fluid; Cm: capacitance of cell membrane; r: right side

Table 2
Measurements of Equivalent Resistivities of Extra- and Intracellular Fluid in the Legs of Postoperative Patients with Leg Edema (Group 2) Using a Multifrequency Impedance Meter

Patient No.	Age (years)	Height (cm)	Weight (kg)	Side Examined	Circum-ference (cm)	RE (Ω.cm)	RI (Ω.cm)	Cm (nF/cm)	RI/RE
11	54	153	45	E	33.0	128	1035	1.1	8.1
12	60	148	44.5	E	30.0	197	491	4.2	2.4
13	65	161	41	E	31.5	209	811	2.2	3.9
14	55	154	69	E	35.0	265	632	2.2	2.4
15	43	158	75	E	40.5	316	704	3.0	2.2
16	67	153	55	E	35.5	266	785	2.3	3.0
17	60	159	70	E	48.0	138	1220	2.0	8.8
18	66	151	58.5	E	42.0	205	1030	2.7	5.0
19	59	156	70	E	41.5	259	742	4.3	2.9
20	54	151	49	E	33.2	194	1050	2.7	5.4
Mean	53.8	154.4	57.7		36.9	218	850	2.7	4.4
± SD	7.2	4.1	12.6		5.8	59	226	1.0	2.4
(n=10)									

E: edematous side. See *Table 1* for other acronyms.

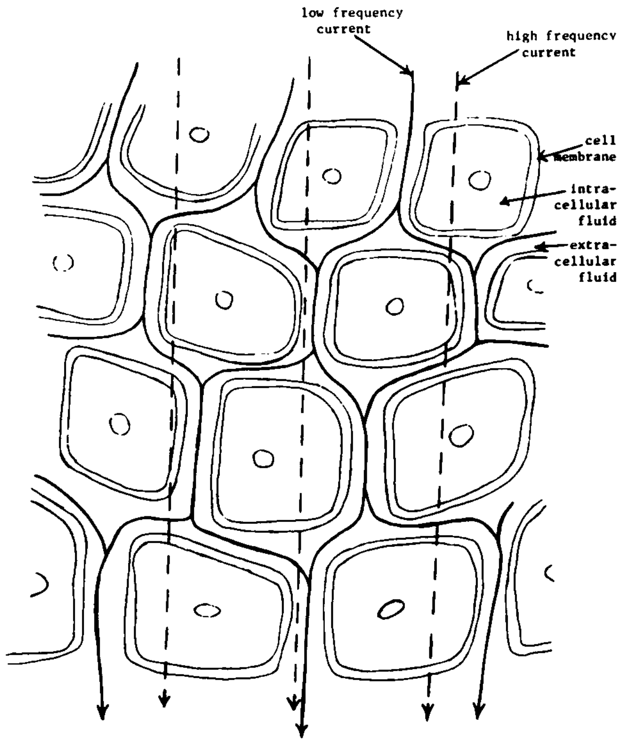

Fig. 1. Schematic diagram of tissues and current flow (5).

months. The patient groups were matched in pairs for age, height and body weight, and the study was performed with consent of each subject.

A multifrequency impedance meter developed by Haeno et al. was used (3,5,6). The frequency characteristics and changes in electrical impedance of living tissues are associated with three kinds of dispersion, termed α, β, and γ dispersion (7). β dispersion is manifest as a structural relaxation which occurs at radio frequencies between 10 KHz and 10 MHz. When a low frequency voltage is applied to the tissue, the current flows mainly through extracellular fluid because the impedance of the cell membrane is substantial at low frequencies. With increased frequency, the impedance of the membrane decreases and current is able to flow through both extra- and intracellular fluids. Therefore, measurements taken at low frequencies provide information about extracellular fluid, whereas those taken at high and low frequencies yield data about intracellular fluid *(Fig. 1)* (5). When the applied current is within the range of 1 to 500 KHz, the electrical properties of tissue can be represented as an R-C circuit composed of Re, Ri and parallel membrane capacitances (Cm) *(Fig. 2a, 2b)* (5). Re and Ri are proportional not only to the resistivity of extra- and intracellular fluid, but also to the tissue shape which may be expressed as the effective ratio of fluid to the sum total of all other extra- and intracellular substances. Any changes of shape depend primarily on changes in fluid volume.

In order to compare results obtained from different individuals, it was necessary to "normalize" the data. RE and the equivalent resistivity of intracellular fluid (RI) were calculated assuming that the volume of a leg between the two voltage electrodes was a cylinder with cross-sectional area S and length L, as follows:

$$RE = Re. S/L \quad (I)$$
$$RI = Ri. S/L \quad (II)$$

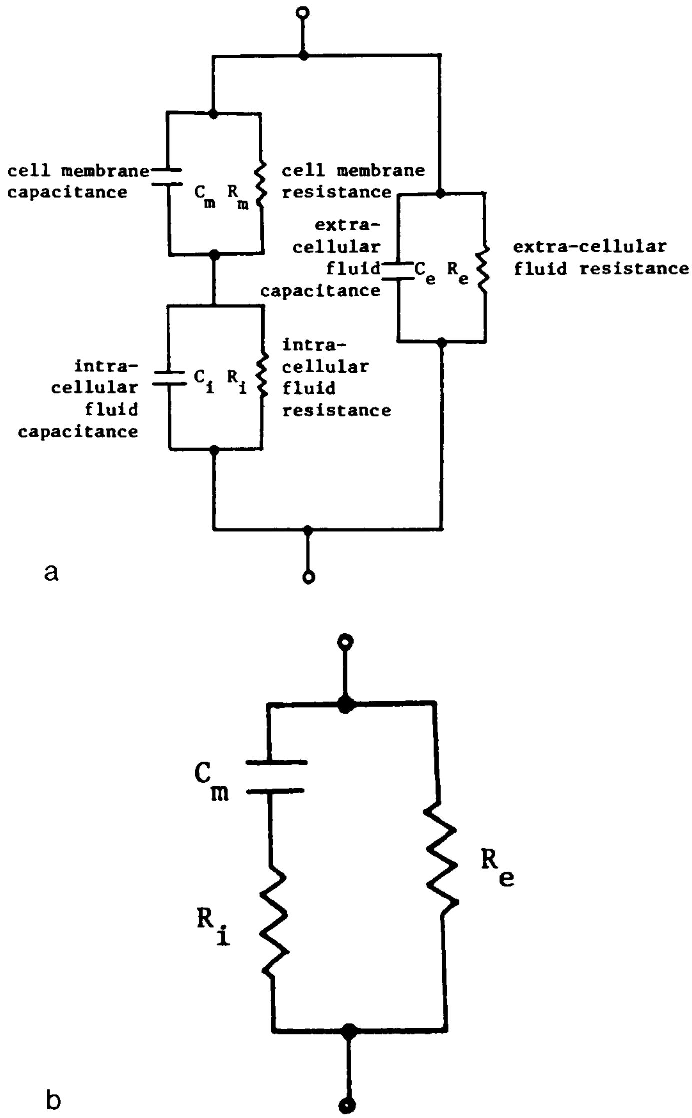

*Fig. 2. Equivalent circuit of a cell or a tissue (5). (**a**) Equivalent circuit for a cell. (**b**) Simplified circuit.*

Alternatively, RE and RI can be represented as,

$RE = \rho e.(S/Se)$ (III)

$RI = \rho i.(S/Si)$ (IV)

Where ρe and ρi are the real resistivities of the extra- and intracellular fluid, respectively, and Se and Si are the effective areas of extra- and intracellular fluid within S, respectively.

Since the real resistivities ρe and ρi are nearly identical in many individuals, RE and RI are mainly affected by changes in the ratios S/Se and S/Si, respectively.

From formulae (III) and (IV),

$Se/Si = \rho e/\rho i \cdot RI/RE = K \cdot RI/RE$ (V)

Measurements were made using four electrodes. Current electrodes were placed around the lower thigh and just above the ankle. One of the two rectangular voltage electrodes (2.4cm) was set 3cm below the head of the fibula with the

Table 3
Sequential Measurements of Equivalent Resistivities of Extra- and Intracellular Fluid in Both Legs of Four Nonedematous Patients

Patient No.	Leg Examined	Circumference (cm)	RE (Ω.cm)	RI (Ω.cm)	Cm (nF/cm)	RI/RE
2	r	32.5	229	1040	2.8	4.5
	l	31.8	244	1040	3.1	4.3
3	r	27.9	211	735	3.1	3.5
	l	27.8	213	799	2.8	3.8
4	r	35.9	289	869	3.1	3.0
	l	36.0	296	790	3.3	2.7
10	r	32.6	348	603	4.3	1.7
	l	32.6	318	647	4.7	2.0
Mean	r	32.2	269	812	3.3	3.2
± SD		3.3	62	187	0.7	1.2
Mean	l	32.1	268	819	3.5	3.2
± SD		3.4	48	163	0.8	1.0
P (n=4)		NS	NS	NS	NS	NS

l: left side. See *Table 1* for other acronyms.

other also on the lateral aspect but 10cm more distal. Both voltage electrodes were thus positioned on an imaginary straight line connecting the head of the fibula and the lateral malleolus. Circumference was measured at the midpoint between the two potential electrodes.

The study was carried out with patients lying supine for at least several minutes. In four of ten patients in Group 1 and in nine of ten patients in Group 2, measurements were made on both legs *(Tables 3,4)*. Seven out of ten in Group 1 and three out of ten in Group 2 had measurements repeated with the leg raised at a 45° angle from the hip joint. Thereafter, data were collected while the subjects were standing. In seven Group 1 patients and three Group 2 patients, measurements were made while the subjects were standing on both legs *(Tables 5,6)*.

Statistical treatment of the data was by paired or unpaired t-test.

RESULTS

As shown in *Tables 1 and 2*, there were significant differences ($p<0.05$) between Groups 1 and 2 in the means of circumference, RE, and Cm. However, no significant differences were found in the means of RI and RI/RE between the two groups. For all 20 patients, the correlation coefficients between circumference/body weight, and RE and RI/RE were -0.652 and 0.458, respectively. Both values were statistically significant ($p<0.01$, $p<0.05$).

Significant differences were found in the means of circumference, RE, Cm and RI/RE between the edematous and unaffected legs of nine Group 2 patients in whom sequential measurements were made on both legs. However, no significant differences were found in the means of these indices between the four Group 1 subjects who had sequential measurements *(Tables 3,4)*. Correlation coefficients between the ratio of cross-sectional area of the legs, and both RE and RI/RE in these 13 patients were -0.614 and 0.805, respectively. These values were statistically significant ($p<0.05$, $p<0.001$).

The changes in RE, RI, Cm, and RI/RE resulting from raising the leg or standing are depicted in *Tables 5 and 6*. In Group 2 as in Group 1, the differences between the mean RE and RI/RE with the leg raised and while standing are not significant on the edematous leg but are

Table 4
Sequential Measurements of Equivalent Resistivities of Extra- and Intracellular Fluid in Both Legs of Nine Edematous Patients

Patient No.	Leg Side Examined	Circumference (cm)	RE (Ω.cm)	RI (Ω.cm)	Cm (nF/cm)	RI/RE
11	E	33.0	128	1035	1.1	8.1
	C	29.0	182	708	1.8	3.9
12	E	30.0	197	491	4.2	2.4
	C	30.1	201	464	4.2	2.3
13	E	31.5	209	811	2.2	3.9
	C	29.5	222	839	1.9	3.8
15	E	40.5	316	704	3.0	2.2
	C	38.7	317	735	3.2	2.3
16	E	35.5	266	785	2.3	3.0
	C	34.6	252	635	2.4	2.5
17	E	48.0	138	1220	2.0	8.8
	C	36.8	234	659	3.2	2.8
18	E	42.0	205	1030	2.7	5.0
	C	33.9	310	723	2.7	2.3
19	E	41.5	259	742	4.3	2.9
	C	39.0	259	762	4.9	2.9
20	E	33.2	194	1050	2.7	5.4
	C	30.0	234	758	3.7	3.2
Mean	E	37.2	212	874	2.7	4.6
± SD		6.0	60	225	1.0	2.4
Mean	C	33.5	246	698	3.1	2.9
± SD		4.0	45	106	1.0	0.6
P (n=9)		< 0.01	< 0.05	NS	<0.05	<0.025

C: contralateral side. See *Table 1* for other acronyms.

different on the contralateral (normal) leg ($p<0.025$ and $p<0.05$, respectively).

DISCUSSION

Clinical methods to quantify peripheral edema include the measuring of leg circumference, ascertaining the depth of pitting (8) and computed tomography (9-12). While evaluating an impedance cardiograph to measure stroke volume (13) in a patient with nephrotic syndrome complicated by anasarca, Watanabe found that electrical impedance (Zo) of the thorax increased with resolution of extensive edema on the chest wall without a notable change in the chest x-ray. Measurement of Zo was then examined in the edematous legs of a patient with uterine cancer. Zo/L varied with changes in depth of pitting and circumference of the extremity (1,2). When carried out on 34 patients with various edema states, Zo/L was low in those who exhibited overt edema (1). However, patients with slight edema displayed a wide range of values which overlapped with that of controls.

On the other hand, Haeno et al. (3) noted an increase in RE following hemodialysis as monitored by a specially designed multifrequency impedance meter. In 1984, Watanabe (1) measured leg impedance, in cooperation with Haeno et al., using the same apparatus in patients with a variety of edemas. The results indicated that RE and RI/RE as represented by formulae (III) and (V) (see Materials and Methods) were useful to estimate the severity of edema in patients with lymphedema where this could not be determined from the depth of pitting.

In this study, the difference in mean

Table 5
Comparison of the Change in Equivalent Resistivities of Extra- and Intracellular Fluid After a Change in Leg Posture in Seven Nonedematous Patients

Patient Number	Side Examined	RE (Ω.cm) raised	RE (Ω.cm) standing	RI (Ω.cm) raised	RI (Ω.cm) standing	Cm (nF/cm) raised	Cm (nF/cm) standing	RI/RE raised	RI/RE standing
1	r	245	204	703	901	3.8	3.8	2.9	4.4
2	l	278	222	967	1150	3.1	3.4	3.5	5.2
3	r	237	191	767	746	3.2	3.7	3.2	3.9
4	r	338	256	791	946	3.0	3.1	2.3	3.7
5	r	288	224	630	742	3.8	4.6	2.2	3.3
7	r	236	206	843	1030	3.0	3.3	3.6	5.0
10	r	396	265	575	728	3.2	5.2	1.5	2.8
Mean ± SD (n=7)		288±60	224±27	754±132	892±163	3.3±0.4	3.9±0.8	2.7±0.8	4.0±0.9
		p<0.005		p<0.005		p<0.05		p<0.005	

See *Table 1* for acronyms.

RE between the edema and non-edema groups is significant and suggests that the amount of extracellular fluid is higher in edematous leg tissue in Group 2. The differences in mean RE and RI/RE between the edematous and unaffected leg in nine patients of Group 2 demonstrates the utility of the method, although in many patients RE values of the edematous leg in Group 2 overlap with those of Group 1 *(see Table 4)*. On the other hand, as shown by the change in RE following a shift in leg position *(see Tables 5,6)*, RE is partially related to leg intravascular fluid volume. The difference in RE following a shift in leg position between edematous and unaffected legs in Group 2 could be explained by a decrease in pooled blood volume in the swollen leg with diminished distensibility of the vascular bed secondary to lymphedema. The advantages of this impedance method are that it can be carried out at the bedside, measurements are easy to repeat and involve no risk to the patient, and it is applicable to non-pitting edema as with lym-

Table 6
Comparison of the Change in Equivalent Resistivities of Extra- and Intracellular Fluid After a Change in Leg Posture in Three Edematous Patients

Patient Number	Side Examined	RE (Ω.cm) Raised	RE (Ω.cm) Standing	RI (Ω.cm) Raised	RI (Ω.cm) Standing	Cm (nF/cm) Raised	Cm (nF/cm) Standing	RI/RE Raised	RI/RE Standing
18	E	212	191	1130	1330	2.3	2.5	5.3	7.0
	C	331	268	739	858	2.6	3.7	2.2	3.2
19	E	276	225	726	772	4.0	3.9	2.6	3.4
	C	278	216	798	996	4.7	4.5	2.9	4.6
20	E	202	192	888	1500	2.7	1.3	4.4	7.8
	C	254	223	808	1380	3.1	1.1	3.2	6.2
Mean ± SD	E	230±40	203±19	915±202	1201±381	3.0±0.9	2.6±1.3	4.1±1.4	6.1±2.3
		NS		NS		NS		NS	
Mean ± SD	C	288±39	236±28	782±37	1078±270	3.5±1.1	3.1±1.8	2.8±0.5	4.6±1.5
(n=3)		p<0.025		NS		NS		p<0.05	

See *Table 1* for acronyms.

phatic obstruction.

Computer tomography (CT) can detect changes in the ratio of muscle to subcutaneous tissues and can also localize stagnant tissue fluid in cross-sections (9-12). However, CT is unable to monitor increases in extra- and intracellular fluid when the subcutaneous tissue space enlarges.

This study revealed no significant difference in mean RI between the non-edema and edema groups. However, the RI values were higher than those previously found in healthy young males (1,5,6). A higher RI in an older subject may relate to such factors as increased fat deposition or skeletal muscle atrophy. Increase in RI and RI/RE following a shift in leg posture *(see Table 5)* may relate, at least in part, to a decrease of intracellular space per unit of leg volume with the gravitationally-induced increase of local blood volume. Haeno (3) and Kanai (5,6) previously observed an increase in Cm after hemodialysis, and significant difference in mean Cm between the two groups studied here needs further investigation.

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