

Impedance Parameter Variations at Intravenous (IV) Infiltration Using Bioelectrical Impedance: A Pilot Study

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ABSTRACT

Infiltration is one of detrimental problems occurring in nursing or medical settings. Early detection of infiltration is essential to minimize the risk of injury from infiltration. To perform a preliminary study on the point of care and automated infiltration detection system, bioelectrical impedance was investigated using bioelectrical impedance analyzer. We would like to report experimental results that allow impedance parameters to effectively distinguish infiltration. Electrodes were attached to both sides of the transparent dressing on the fusion site where IV solution was being infused. Then, impedance parameters before and after infiltration were measured as a function of time and frequency. The experimental results are as follows. After infiltration was intentionally induced by puncturing the vein wall with a needle, the resistance gradually decreased with time. That is, when an alternating current having a frequency of 20 kHz was applied to the electrodes, the resistance gradually decreased with time, reflecting the accumulation of IV solution in the extracellular fluid since the current could not pass through the cell membrane. Impedance parameters and equivalent circuit model for human cell were used to examine the mechanism of current flow before and after infiltration, which could be used for early detection of infiltration.

Key words: Infiltration, IV Infusion, Bioelectrical Impedance, Resistance, Reactance, Capacitance, Bioelectrical Impedance Vector Analysis (BIVA)

1. INTRODUCTION

Intravenous (IV) cannulation is a technique in which a cannula is placed inside a vein to provide venous access. Venous access allows admin-

istration of fluids, medications, parenteral nutrition, chemotherapy, and blood products as well as sampling of blood [1]. The Infusion Nurses Society's National Standards of Practice requires that a nurse who administers IV medication of fluid

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should know its adverse effects and appropriate interventions to take before starting the infusion [2]. IV catheters frequently fail before the end of treatment because of irritation of the vein (phlebitis) with symptoms including pain, swelling, redness, occlusion, and a palpable venous cord. Of the 200 million peripheral intravenous catheters estimated to be inserted each year in the US alone, if even 15% are needed for more than 3 days, then a change to clinically indicated replacement would prevent up to 6 million unnecessary intravenous catheter insertions [3]. Peripheral IV catheter-related bloodstream infection is a less frequent but serious complication, occurring in about 0.1% of intravenous catheters or 0.5 per 1000 catheter days [4]. IV infiltration and extravasation (ie., infusion leaking out of the blood vessel) are frequently observed in the clinical setting as detrimental complications related to intravenous injection [2,5]. Infiltration and extravasation are risks of intravenous administration therapy involving unintended leakage of solution into the surrounding tissue. Consequences range from local irritation to amputation [6]. Infiltration and extravasation can occur in any patient during a course of IV therapy. Extravasation can be a stressful event for even the most experienced practitioner [7]. While immediate action using appropriate measures (ie, dilution, extraction, antidotes, and supportive treatments) can decrease the need for surgical intervention, many injuries may be prevented by following established policy and procedures. However, timely surgical intervention when needed can prevent more severe and diverse outcomes [6,8]. Recently, studies have been conducted to reduce infiltration in nursing environments by educating nurses dealing with IV solutions [9,10]. In addition, the ratio of the diameter of the blood vessel and the catheter between the infiltration group and the no-infiltration group was obtained using ultrasound. The diameter of the blood vessel was reported to be 3.3 times than that of the catheter where health care professionals can

identify veins appropriate [11].

The detection of infiltration and extravasation during peripheral venous treatment has been performed using a variety of optical, electrical, thermographic, and ultrasonographical methods [12–15]. For illustration, an intravenous infiltration detection apparatus was proposed for monitoring intravenous failure, which applies an optical method coupled with fiber optics and algorithm for non-invasive detection of intravenous infiltration induced at the punctured site of IV injection [12]. When infiltration was intentionally induced, resistance was reported to be decreased by 10% in 20 seconds. Early detection system (iv Watch Model 400) of peripheral IV infiltration and extravasation events through continuous monitoring of the IV site was proposed using near infrared light [13]. The optical sensor could detect the difference in reflectance of light due to infiltration in the subcutaneous tissue beneath the needle. A novel proof-of-concept system that uses non-invasive sensing in conjunction with a low-power embedded computing platform was proposed to deliver continuous infiltration monitoring around the IV catheter site [14]. This kind of system could be able to detect an infiltration by non-invasively monitoring for known symptoms: swelling of soft tissue and increased skin firmness; these symptoms can be sensed by measuring skin stretch and local bioimpedance. However, only limited information about the infiltration could be obtained in these methods because they measure only the difference of reflected light from transparent liquid accumulated around IV site before and after infiltration. Recently, infiltration in subcutaneous edema patients was detected by thermographic and ultrasonographical method [15]. However, this technology is complex and costly, and is not readily available on the bedside of hospitals.

To solve the shortcomings of the existing systems, an early detection system of IV infiltration is imperative for a simple, reliable, inexpensive, and

noninvasive method capable of monitoring IV sites. From the point of view, the bioelectrical impedance analysis (BIA) is a safe, practical, and non-invasive method for measuring components of biological tissues and biological materials [16,17]. BIA relies on the conduction of radio-frequency electrical current by the fluid (water, interstitial fluid, and plasma), electrolytes, and ionic conductivity or permeability of cell membrane in the tissue. BIA has been currently utilized to diagnose the diseases as well as assess the hydration status, body composition, muscle-fat ratio, obesity degree, lean balance, edema, and nutritional status of the patients [18,19].

In this study, the impedance (resistance, reactance) was measured as a function of time during infusing intravenous (IV) solution into the vein. In order to monitor IV site during infiltration, compared to IV proper infusion, impedance was measured as a function of time and frequency before and after infiltration. IV infiltration into the surrounding subcutaneous tissue after infiltration was described using equivalent circuit of the human cells and impedance parameters such as resistance, reactance, capacitance, and bioelectrical impedance vector analysis (BIVA). The relative resistance, which is the ratio of resistances to resistance at 20 kHz, and BIVA at 50 kHz could be applied to early detection of infiltration, well reflecting the quantitative reduction of the impedance (resistance, impedance vector) with infiltration. We aim to report our experimental results that allow impedance parameters to effectively distinguish infiltration.

2. THEORY

2.1 Equivalent Circuit of Cell Membrane, ICF, and ECF

Total body water (TBW) account for 60% of the mass (also weight) depending on the age, the sex, and the obesity. The intracellular fluid (ICF) accounts for about 40% of total body water (TBW)

and the extracellular fluid (ECF) about 20% of TBW. In addition, the interstitial fluid (ISF) occupies about 75% of ECF and the plasma about 25% of ECF. Despite having lower protein content, the composition of ISF is similar to that of the plasma. Cells constituting the human organ consist of ICF and ECF that behave as an electrical conductor, and the cell membrane acts as an electrical capacitor [16].

Fig. 1 indicates an equivalent circuit of the cell model [20], and Table 1 lists descriptions of the indicated symbols.

Since the resistance R_m and the capacitance C_m of the cell membrane are connected in parallel, the reactance X_c of the cell membrane in Fig. 1 can be expressed by Eq. (1):

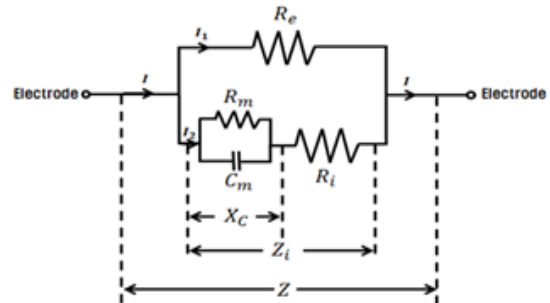


Fig. 1. Equivalent circuit model of cell consisting of ECF (R_e), the cell membrane (C_m), and ICF (R_i).

Table 1. Meaning of symbols indicated in Fig. 1

Symbol	Description
C_m	Capacitance of cell membrane
R_m	Resistance of cell membrane
R_e	Resistance of ECF
R_i	Resistance of ICF
X_c	Reactance of cell membrane
Z_i	Impedance of X_c and R_i
Z	Impedance of Z_i and R_e
I	Current through both ECF and ICF
I_1	Current through primarily ECF
I_2	Current through both cell membrane and ECF

$$X_c = \frac{1}{\frac{1}{R_m} + j\omega C_m} = \frac{R_m}{1 + j\omega R_m C_m} = \frac{R_m}{1 + j2\pi f R_m C_m} \quad (1)$$

Impedance (Z_i) of the cell membrane and ICF can be expressed by Eq. 2:

$$Z_i(j\omega) = R_i + X_c = R_i + \frac{1}{\frac{1}{R_m} + j\omega C_m} = R_i + \frac{R_m}{1 + j\omega R_m C_m} \quad (2)$$

Total impedance (Z) having a coupling structure in parallel with the extracellular fluid (ECF) with the intracellular fluid (ICF) in series with the cell membrane (X_c) can be expressed by Eq. (3):

$$Z = R + iX_c \quad (3)$$

2.2 Bioelectrical Impedance Vector Analysis (BIVA)

Bioelectrical Impedance Vector Analysis (BIVA) illustrates the relationship of resistance (R) and reactance (X_c) normalized per height as a bivariate vector in the R/H vs. X_c/H graph [21]. The normalization for height allows for the length of the conductor and thus provides a qualitative measure of soft tissue that does not depend on body size. The impedance vector (length, direction) in BIVA provides valuable information about hydration status, muscle mass and cell membrane integrity. The length of BIVA indicates hydration status from fluid overload (decreased resistance, short vector) to exsiccosis, which is insufficient intake of fluids (increased resistance, longer vector) [22]. The direction (migration sideways) of BIVA due to low or high reactance indicates decrease or increase of muscle mass in tissues. Significant vector displacement was observed with increasing disease severity [23,24]. BIVA approach has gained attention as a useful tool to assess and monitor the hydration and the nutrition status in patients. BIVA could be used for routine monitoring of the variation in body fluids, nutritional status of individuals, and for representing a clinically useful procedure [25]. BIVA has been used effectively to assess the hydration status in the human body. In patients

with renal insufficiency in particular, BIVA has been validated as an effective method for assessing the hydration status [26] and identify patients with a critical fluid overload [27] which is associated with increased risk of mortality. Pillon et al. demonstrated that shorter vector length as a measure of inadequate ultrafiltration was associated with increased mortality, and that the increase in relative risk with shorter vector length was independent of age, sex, ethnicity, diabetes, length of time on dialysis, albumin, creatinine, haemoglobin, ferritin, and even phase angle [28].

3. METHOD

3.1 Subjects

The study was carried out in small exploring clinical trials led by researchers. The subjects were 2 males with a mean age of 61.0 years (± 2.0 years), an average height of 168.0cm (± 3.0 cm), an average mass of 68.0kg (± 3.0 kg), and an average body mass index (BMI) of 24.23 (± 0.34 kg). Prior to participation in this study, the purpose and method of the study was explained to the subjects, and their written consents were obtained. In this study, two research subjects participated in the total 7 trials as a small research study led by researchers. This study was approved by the IRB committee of Pusan National University Yangsan Hospital (IRB No. 03-2016-017).

3.2 Peripheral intravenous injection and induced infiltration

The BIA equipment was checked before measurement against the calibration circuit standard with known resistance and reactance values to ascertain the accuracy of measurement. After inserting peripheral IV catheter into the vein, the transparent dressing (10.2 cm \times 7.4 cm, Sewoon LTd, Korea) was attached to ensure the infiltrated vein accurately with the naked eyes. Ag/AgCl medical electrodes (2223H, 3M, Korea) were attached to both sides of the transparent dressing on the in-



Fig. 2. Circular electrodes used to measure the impedance to detect vein-induced infiltration in the left forearm. Outside band electrodes are for detecting infiltration with another measuring device.

fusion site as shown in figure 2. After inserting PIV catheter into the vein on inner forearms of subjects, the infiltration was deliberately induced during measuring BI. Then, the transparent dressing was immediately attached on the punctured infusion site to visually observe the swelling tissue around infiltrated vein. BI was measured over time before and after infiltration, using bioelectrical impedance spectroscopy (called Vector) developed by Kim [29]. Alternating current (800 μ A) having 8 different frequencies (20, 50, 100, 200, 300, 500, 700, and 1000 kHz) was applied to electrodes to measure BI as a function of time before and after infiltration. This study was a researcher-led small-scale exploratory study in which two subjects participated in seven experiments.

4. RESULTS AND DISCUSSION

4.1 RESULTS

Fig. 3 shows the resistance as a function of time for a frequency ranging from 20 to 1,000 kHz during infusing the IV saline solution into the vein. BI (before infiltration) indicates when IV solution is properly infused. AI (at infiltration) indicates when the infiltration was intentionally induced. The measured values are the average of the seven measurements of two subjects. The resistance de-

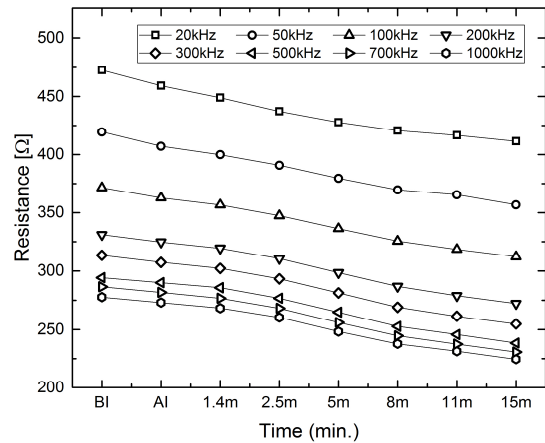


Fig. 3. Resistance as a function of time and frequency. The resistance gradually decreases over time. BI (before infiltration) indicates when IV solution is properly infused. AI (at infiltration) indicates when the infiltration occurs.

creased with increasing time and frequency. At each frequency, the resistance gradually decreased over time (proportional to the amount of IV solution), reflecting IV solution (also blood components) accumulated in ECF. The decrease in resistance over time for all frequencies after infiltration explains more precisely the mechanism of infiltration mechanism than the simple reduction of impedance or reflected light after infiltration performed by other researchers [11,13].

Whether a cell membrane acts as a capacitor or resistor depends on the frequency of the applied current. When an alternating current (AC) having a frequency of 20 kHz ($8.4 \times 10^{-11} eV$) 50 kHz was applied to IV infusion site, the resistance was comparatively large because the current passed primarily through ECF (adipose tissue containing about 80% fat). Only a small amount of the current finds “the path of least resistance” through a capillary [30]. At 50 ($2.1 \times 10^{-10} eV$), decreasing impedance over time reflects IV saline solution accumulating in ECF after infiltration. Since AC having a frequency higher than 50 kHz is able to pass through the cell membrane, this allows the measurement of fluid status inside of cells (ICF) as well

as outsides of cells (ECF). In addition, ICF (70%) has a larger intracellular cross-sectional area than adipose-rich ECF (30%) in subcutaneous tissue. Thus, the resistance decreases further with increasing frequency.

Fig. 4 shows the relative resistance obtained by dividing the resistance measured over after infiltration by the resistance measured at 20 kHz before infiltration. This is indicative of a reduction in resistance that is proportional to IV saline solution accumulated in ECF of subcutaneous tissue due to infiltration. When infiltration was intentionally induced, the resistance was 2.7% less than that before infiltration. Since the amount of accumulated fluid increases over time, the resistance decreased relatively rapidly until 8 minutes. Thereafter, the resistance decreases gradually since there is less accumulation of IV solution due to the pressure of the surrounding subcutaneous tissues.

Reactance (X_c) is the measure of a cell membrane's ability to slow a current [30]. For example, cell membrane can store a charge for a short period of time, thus slowing the current. Whether a cell membrane acts as a capacitor or a resistor is dependent upon the frequency of the current applied. At low frequency lower than 50 kHz, current is

stopped by cell membrane. The membranes are resistors, as no current conducts through them. Therefore, at low frequencies, any current conducted through a body passes through ECF only. Current with a frequency higher than 50 kHz is able to pass through cell membranes. This allows the measurement of substances inside of cells as well as outside of cells.

Fig. 5 shows the reactance as a function of time and frequency for a frequency ranging from 20 to 1000 kHz. When infiltration induced during infusing IV saline solution into the vein, the reactance decreases significantly and then decreases gradually. Reactance decreases markedly when infiltration occurs since the ability of the cell membrane to stop the current decreases. The decrease in reactance was distinctly observed at low frequencies.

Body capacitance is the absolute amount of energy storage of the body due to intact cellular membranes. A high capacitance indicates that human body stores energy effectively. A low capacitance would suggest that cells are having trouble storing energy. Normal values are between 500 to 1000 pF. The cell membrane acts as a capacitor when a current having high frequency is applied. At this time, the capacitance is inversely proportional to the applied frequency and reactance as

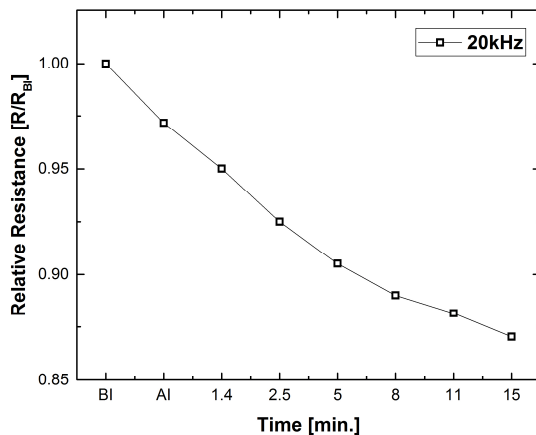


Fig. 4. Relative resistance at 20 kHz as a function of time. The decrease in relative resistance over time reflects the accumulation of IV saline solution in ECF.

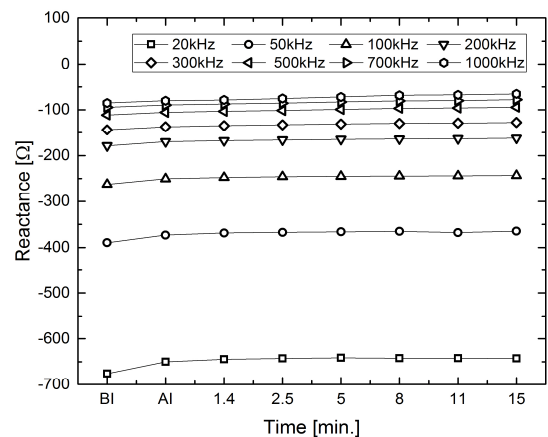


Fig. 5. Reactance (X_c) as a function of time and frequency. A decrease in reactance magnitude due to infiltration is clearly observed at 20 kHz

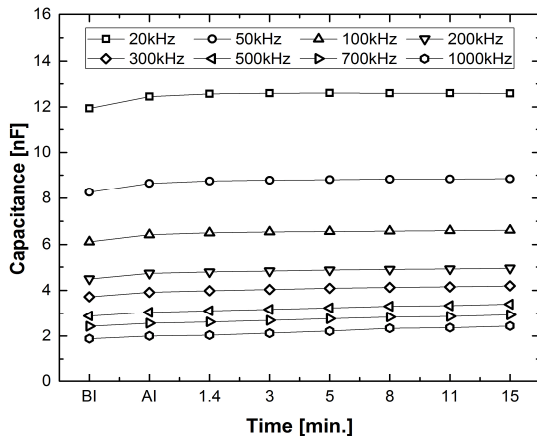


Fig. 6. Capacitance (C_m) of cell membrane as a function of time and frequency. The capacitance of the cell membrane increased significantly at infiltration (AI) and increased gradually thereafter.

follows: $C = 1/2\pi fX_c$. Fig. 6 shows the capacitance as a function of time for each frequency. Capacitance decreases with increasing frequency. The capacitance of the cell membrane increased significantly at infiltration (AI) and gradually increased thereafter. This suggests that saline solution and blood components (red blood cells, white blood cells, platelets, etc.) from the vein are ad-

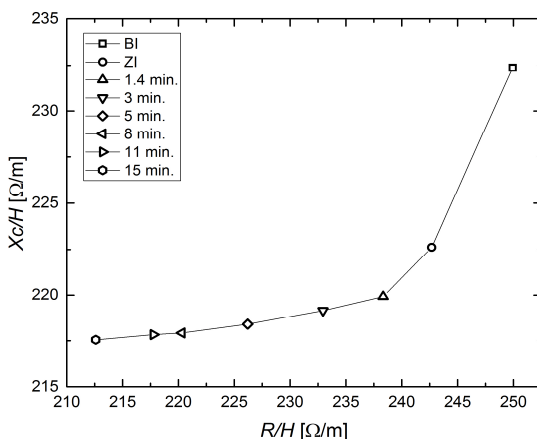


Fig. 7. Migration of impedance vector in bioelectrical impedance vector analysis (X_c/H vs. R/H). When infiltration was induced, the position of the impedance vector shifted significantly to the lower left. This could be used as important data for early detection of infiltration.

sorbed on the cell membrane during infiltration and then increase the capacitance of the cell membrane.

Fig. 7 shows the mean impedance vectors of BIVA, which is the reactance (X_c) divided by height (H) to the resistance (R) divided by height (H), for a frequency of 50 kHz. When infiltration was induced during IV infusion, the impedance vector moved in the lower left due to IV solution leaking from the vein into the surrounding cutaneous tissue, weakening the cell membrane. When IV solution was accumulated in the subcutaneous tissue due to infiltration, X_c/H and R/H were simultaneously decreased and the impedance moved downward to the left significantly. The migration of the impedance vector in BIVA could provide a useful tool for the early detection of infiltration.

4.2 DISCUSSION

Infiltration (or extravasation) detection systems have been developed using thermal, electrical, and optical methods. For example, the extravasation of fluid during infiltration was detected using bioelectrical impedance. For example, the electrodes were attached to five dogs' legs and ion and non-ion contrast agents were injected. When the impedance was simply decreased, it was judged that there was a leak in the blood vessel. In another experiment, infiltration was also confirmed by simply comparing the reflectance of light reflected from the skin before infiltration and the reflection of light reflected from the skin after infiltration. That is, when infiltration occurred, the reflectance of light (visible light or infrared light) reflected from the skin surface due to the IV solution leaking out of the vein was remarkably reduced. In contrast, impedance experiment in this study was performed by intentionally puncturing the vein with the needle while infusing IV solution into the subject's vein. Bioelectrical impedance was measured in the frequency range from 20 kHz to 1000 kHz before and after infiltration. The bioelectrical impedance parameters and the equivalent circuit

model in ECF of human cells were used to quantitatively investigate the accumulation of IV saline solution during infiltration. In addition, the variation of the impedance vector due to the leakage of saline solution was reflected in BIVA diagram. Until this time, optical data for the infiltration was approximately obtained using the reflectance from the skin. However, these methods could not provide the useful information on the accumulation of infiltrating IV solution into the skin/subcutaneous tissues or pathological/physiological information that IV solution and blood components affect skin or subcutaneous tissues.

In this study, IV solution penetrating from the vein into the surrounding subcutaneous tissue during infiltration was analyzed using the impedance parameters (resistance, reactance, and capacitance) and BIVA plot. When the infiltration occurred, the resistance and reactance gradually decreased as a function of time. In addition, using impedance parameters measured at different frequencies from 20 to 1000 kHz and an equivalent circuit model of the human cell, IV solution leaking out of the vein was confirmed to be accumulated in ECF. Furthermore, when infiltration occurred during IV infusion, the impedance vector shifted in the lower left due to IV solution leaking from the vein into the skin and subcutaneous tissue, weakening the cell membrane. A significant displacement of the impedance vector due to reduced X_c/H and R/H was observed in BIVA diagram with increasing IV solution. These phenomena are in good agreement with the findings reported by Nescolarde et al. [31]. The resistance for more severe injury was further decreased (11.9% in grade 1, 20.6% in grade 2, 23.1% grade 3) compared to the non-injury (68 Ω). The migration of impedance vectors in BIVA allows early detection of infiltration during IV infusion.

5. CONCLUSION

In this study, bioelectrical impedance (resistance,

reactance) was measured to detect IV infiltration before and after infiltration. The resistance and reactance was measured as a function of time and frequency during infusing IV solution into the vein, using BIA. When infiltration was intentionally induced, the resistance and the reactance decreased gradually over time (proportional to an amount of injection solution). Using an equivalent circuit model and impedance parameters, IV solution leaking out from the vein was confirmed to be accumulated in ECF. In addition, when an alternating current (AC) having a frequency below 50 kHz ($2.1 \times 10^{-10} \text{ V}$) was applied to IV infusion site, the resistance was comparatively large because the current primarily passed through ECF (adipose tissue containing about 80% fat). Only a small amount of the current finds "the path of least resistance" through a capillary [30]. At 20 kHz ($8.4 \times 10^{-11} \text{ V}$), decreasing impedance over time reflects IV solution accumulating in ECF after infiltration. On the other hand, when a current having a frequency higher than 50 kHz ($2.1 \times 10^{-10} \text{ V}$) was applied to the IV site, the impedance was gradually decreased because the applied AC was strong enough to penetrate the cell membrane and flew in both ECF and ICF.

The experimental results obtained using the impedance parameters and BIVA for early detection of infiltration are as follows. First, the resistance decreased with increasing time (proportional to amount of IV solution). At each frequency, the resistance gradually decreased with time, indicating IV solution (also blood components) accumulated in ECF (including ISF). Second, reactance decreased significantly at infiltration and gradually decreased after infiltration. It seems that the infiltration degrades the structural/physio-pathological function of cell membrane. Third, the capacitance of the cell membrane gradually increased due to infiltration. IV solution and blood components leaking from the vein during infiltration is believed to increase the capacitance of cell mem-

brane. Fourth, BIVA diagram indicated that as infiltration progressed, the impedance vectors shifted in the leftward to the bottom, reflecting a gradual decrease in resistance and reactance while infiltration. Thus, it was confirmed that the infiltration phenomenon could be detected quantitatively by using the impedance parameters and BIVA. The mechanism of current flow in ECF and ICF through cell membrane and the function of cell membrane according to the frequency could be clarified using impedance parameters and equivalent circuit model of the human cell.

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