

# Early Detection of Peripheral Intravenous Infiltration Using Segmental Bioelectrical Impedance: Preliminary Study

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## ABSTRACT

Early detection of infiltration is one of the most important tasks of nurses to minimize skin damage due to infiltration. For subjects receiving invasive intravenous treatment, the bioelectrical impedance (impedance) were measured in the frequency range of 5 to 500 kHz using bioelectrical impedance spectroscopy (BIS). After attaching electrodes at both ends of a transparent dressing mounted on the skin in which IV solution was infused into the vein, the change in impedance was measured as a function of time and frequency before and after infiltration. The experimental results are described as follows. When IV solution was properly infused into the vein, the impedance was nearly constant over time and decreased with increasing frequency. However, when infiltration occurred, the impedance decreased significantly and thereafter gradually decreased with time. In addition, impedance decreased with time for all applied frequencies. In this study, when IV solution penetrated into the surrounding skin and subcutaneous tissue by infiltration, impedance was quantitatively analyzed for as a function of time and frequency. This suggests a method for early detection of infiltration using BIS.

**Key words:** Intravenous (IV) Infiltration, Early Detection, Bioimpedance, Extracellular Fluid (ECF), Equivalent Circuit of Cell Membrane

## 1. INTRODUCTION

Peripheral intravenous (IV) catheter insertion is a practical technique often used in medicine and nursing to provide therapeutic IV medication [1, 2]. IV infiltration and extravasation are commonly observed in the clinical setting as devastating complications associated with IV injection [3]. Infiltration refers to the accumulation or diffusion of non-effervescent fluid or drugs into surrounding tissues other than the vascular pathway, whereas extrav-

asation refers to the accumulation or diffusion of effervescent fluid or drugs [4]. Infiltration occurs when a catheter tip inserted into peripheral vein penetrates through a weak vessel wall and IV solution being infused through the catheter flows into the surrounding subcutaneous tissues [5]. Extravasation occurs when the osmotic pressure of infused solution is high or the blood vessel walls and surrounding tissues are damaged due to pharmacological factors of the fluid [6].

Researches on infiltration have been carried out

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Receipt date : Jan. 6, 2017, Revision date : Mar. 2, 2017  
Approval date : Mar. 13, 2017

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※ This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and Future Planning (2015R1A2A2A04003415).

by many other researchers [7–8]. Thigpen presented an initial approach to nursing care for peripheral IV infiltrations to guide clinicians based on clinical experience, descriptive studies, and reports from expert committees [7]. Infiltrations are difficult to detect, especially in its early stage. To date, techniques used to detect infiltrations primarily relied on clinical methods, which include visual inspection of the IV site, visual inspection of the connector tube for blood return, and visual and tactile examination of the skin and tissues proximate to the IV injection site for factors such as tissue pressure, color, edema, turgor and temperature [8].

Since early detection of infiltration can help prevent the occurrence of more serious complications that may require surgical corrections, many attempts to detect infiltration and extravasation during peripheral venous treatment have been performed using temperature, ultrasound, microwave, near infrared, and impedance measurement [9]. Since the IV solution entering the vein is either cooled or at ambient temperature, the infiltrated liquid flow can be detected using a thermometer or segment of bandage coated with thermochromic crystal [10]. An IV infiltration detection apparatus coupled with fiber optics and algorithms for tissue optics have also been proposed to monitor intravenous failure [11]. The tissue surrounding the injection site is exposed to a single-wavelength of electromagnetic radiation, and light is collected with only one detector. Changes in the relative intensity of radiation reflected, scattered, diffused or emitted provide a way of monitoring infiltration. IvWatch<sup>TM</sup> was developed to monitor the intravenous infusion site for infiltration [12]. It consisted of two components, a skin contact sensor and an electronic device, connected via two optical fibers. The first optical fiber sends input light to the skin contact sensor whereas the second optical fiber delivers the collected light (output) from the infusion site to the electronic device. As IV solution infiltrates the interstitial space, the density of light

coming from the tissue changes, causing a change in the signal of the light being collected. The presence of infiltrated solution in subcutaneous tissues was obtained from the difference in the measured signals. However, only limited information about infiltration could be obtained with these methods because only the difference in the light reflected from transparent liquid flowing around IV site was measured before and after the infiltration.

To solve existing problems of the current IV infiltration detection systems, the new IV detection system should be able to monitor IV sites in a simple, reliable, inexpensive, and non-invasive way. The bioelectrical impedance analysis (BIA) is a safe, practical, and non-invasive method for measuring components of biological tissues and biological materials [13, 14]. BIA relies on the conduction of radio-frequency electrical current by the fluid (water, interstitial fluid, and plasma), electrolytes, and permeability of cell membrane in the tissue [15]. It has been utilized to diagnose diseases as well as assess the hydration status, body composition, muscle-fat ratio, obesity, lean mass, edema, and nutritional status of the patients [16–19].

In this study, to determine what changes in impedance can occur when the IV solution is injected properly into the vein, impedance was measured as a function of time and frequency during IV infusion into the vein. The two subjects were intentionally stabbed into the vein wall with a needle while receiving IV fluid to induce infiltration. In order to determine the effect of the infiltrated IV solution accumulating in the skin and subcutaneous tissue for impedance changes, impedance was also measured for time and frequency before and after the infiltration. When IV solution was properly infused into the vein, the impedance was almost constant (with some fluctuations) over time for 7 different frequencies. However, when infiltration occurred, impedance gradually decreased because IV solution accumulated in extracellular fluid (including interstitial fluid) in subcutaneous tissues, allowing early

detection of IV detection. The accumulation of IV solution that penetrated from the vein into the surrounding subcutaneous tissue (ie., extracellular fluid) after infiltration was described using bio-impedance and the equivalent circuit of human cell.

## 2. METHODS

### 2.1 Equivalent Circuit of Cell Membrane, ICF, and ECF

A basic understanding of normal body fluid physiology is required to be able to appreciate the nuances of fluid therapy. Total body water (TBW) accounts for approximately 60% of the total body weight depending on sex, age, and obesity. TBW is distributed between the intracellular fluid (ICF) compartment (approximately 66%) and the extracellular fluid (ECF) compartment (approximately 33%). These two spaces are separated by cell membranes. The ECF compartment is further subdivided into intravascular (8% TBW) and interstitial (25% TBW) spaces [20], and these compartments are separated by the capillary wall. The barriers (cell membranes) between the fluid compartments have different permeability to different solutes based on size, charge, and conformation. This selective permeability, along with hydrostatic and oncotic forces (i.e., Starling forces), determines the movement of fluids and electrolytes between the compartments. Cells constituting human organs consist of ECF and ICF that behave as electrical conductors, whereas the cell membrane acts as an electrical resistor and capacitor [21, 22].

Fig. 1 indicates an equivalent circuit of a cell in the human body. Table 1 lists the descriptions of the indicated symbols in Fig. 1. When the frequency of the alternating current applied to the skin of the human body is low, the current flows into ECF (including interstitial space) which is narrow and contains a lot of adipose. So the impedance is measured high. The IV solution flowing out of the vein during infiltration accumulates in

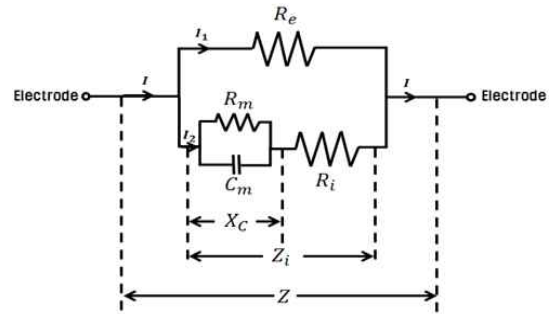


Fig. 1. The human body consists of resistance ( $R_e$ ,  $R_m$ ,  $R_i$ ) and capacitance ( $C_m$ ) connected in parallel or in series. In the parallel model, two or more resistors and capacitors are connected in parallel, with the current passing through the extracellular space at low frequencies and through the intracellular space at high frequencies.

Table 1. Description 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 only ECF
$I_2$	Current through both cell membrane and ECF

the ECF, thereby gradually decreasing the impedance with time. However, when an alternating current having a frequency of 50 kHz or higher is applied to the skin, the current has sufficient energy to pass through the cell membrane, so that the current flows into the intracellular fluid (ICF). The current flows through both the ECF and the ICF, thus lowering the impedance. When the frequency of the alternating current is further increased, the impedance becomes lower since the capacitance of the cell membrane decreases and the current flows freely through ICF.

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 as follows:

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

The reactance ( $X_c$ ) of the cell membrane and the resistance ( $R_i$ ) of ICF connected in series can be expressed as

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

The total impedance ( $Z$ ) of the cell model can be represented as

$$Z = \frac{1}{\frac{1}{R_e} + \frac{1}{Z_i}} = \frac{R_e Z_i}{R_e + Z_i}. \quad (3)$$

The reactance ( $X_c$ ) of the cell membrane depends on the applied frequency. When the frequency of the applied alternating current is high, the impedance ( $Z$ ) decreases because  $X_c$  and  $Z_i$  decrease according to Eqs. (1) and (2). On the contrary, when the frequency of the applied alternating current is low,  $Z$  increases as the opposite phenomenon occurs.

## 2.2 Subjects

In this study, two healthy adults were selected as experimental subjects to conduct a small-scale exploratory clinical trial led by researchers. The impedance experiment on the infiltration was conducted three times for 2 subjects, resulting in a total of 6 measurements. The subjects were 2 males with a mean age of 61.0 years  $\pm$  2.0 years, a mean height of 168.0 cm  $\pm$  3.0 cm, a mean mass of 68.0 kg  $\pm$  3.0 kg, and a mean body mass index (BMI) of 24.23 kg/m<sup>2</sup>  $\pm$  0.34 kg/m<sup>2</sup>. Prior to participation in this study, the purpose and method of the study was explained to the subjects, and their written consents were obtained. This study was approved by the IRB committee of Pusan National University Yangsan Hospital (IRB No. 03-2016-017).

## 2.3 Peripheral IV injection and induced infiltration

After inserting peripheral intravenous (PIV) catheter into the vein, a transparent dressing (10.2 cm  $\times$  7.4 cm, Sewoon LTd, Korea) was mounted on the skin to visualize the leakage of IV solution from vein due to infiltration with the naked eye. Cutaneous electrodes (Bodystat-0525, UK) for applying a current were attached to the inferior region of the left upper arm and to the base of fingers. Electrodes (with 12 cm separation) for collecting the voltage were attached to both sides of the infusion site.

The impedance measurement was conducted at frequency ranging from 5 to 500 kHz using BIS (MultiScan5000, Bodystat Ltd., UK) while applying alternating current (AC) of 800  $\mu$ A to the electrodes. First, BI was measured in 5-minute intervals up to 35 minutes while IV solution was being injected at a rate of 60 ggt/min. into the vein. In addition, after inserting PIV catheter into the vein of inner forearm, an infiltration was intentionally induced by pushing the needle through the vein wall into the subcutaneous tissue. Then, the transparent dressing was immediately attached on the infusion site to visually observe swelling of the tissue around infiltrated site. BI was measured as a function of time during and after infiltration. Alternating current with 7 different frequencies (5, 50, 100, 200, 300, 400, 500 kHz) was applied through the current-injecting electrodes and the voltage between voltage-collecting electrodes was measured to obtain BI. Fig. 2 shows the induced infiltration in the inner forearm of subject during IV infusion.

## 3. RESULTS AND DISCUSSION

### 3.1 Bioelectrical impedance as a function of time during IV infusion

Fig. 3 shows the impedance as a function of time during IV infusion. When IV solution was properly infused into the vein, there was minimal change (with some fluctuations) in impedance over time for 7 different frequencies. When a current with

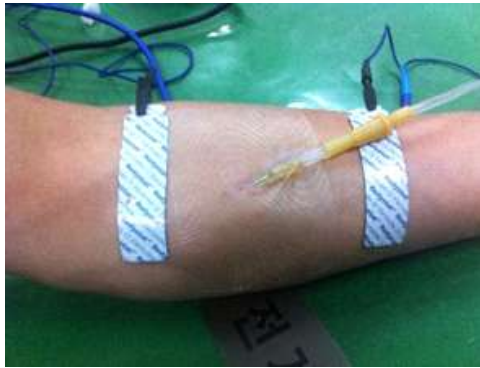


Fig. 2. The infiltration induced in the left forearm of subject during IV infusion.

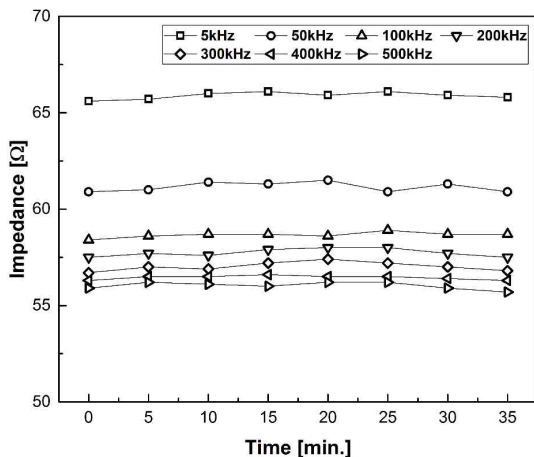


Fig. 3. Bioelectrical impedance ( $Z$ ) as a function of time during IV infusion.

a frequency of 5 kHz was applied to the IV site, the impedance ( $Z$ ) was relatively high (65.0~65.5  $\Omega$ ) because the current flowed only into narrow ECF with adipose tissues. When a current with a frequency of 50 kHz or higher was applied to the IV sites, the magnitude of impedance decreased, but exhibited a constant value over time.

### 3.2 Impedance as a function of frequency during IV infusion

Fig. 4 shows impedance as a function of frequency during IV infusion into the vein through a catheter. Impedance decreased exponentially with increasing frequency, with slight variation over

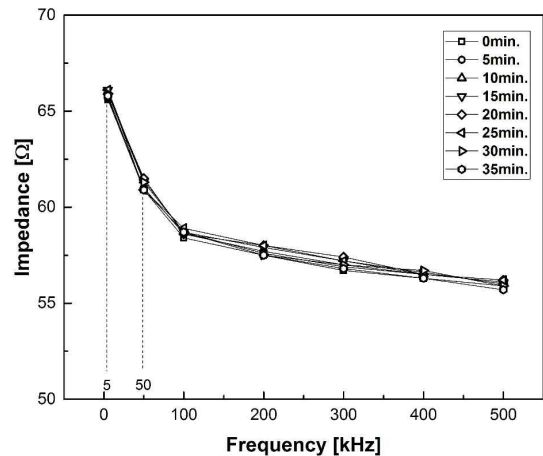


Fig. 4. Impedance as a function of frequency during IV infusion.

time. Impedance decreased significantly between 5 and 50 kHz, and then decreased gradually. At low frequency below 50 kHz, most of the current is stopped at the cell membrane composed of the adipose tissue. Only a small amount of current finds the “path of least resistance” through a capillary [23]. The path of least resistance can be any body component high in water content, including blood, extracellular fluid, and muscle. Therefore, at a low frequency, any current conducted through body is flowing through ECF only. On the other hand, when a current with frequency higher than 50 kHz ( $2.1 \times 10^{-10}$  eV in energy scale) is applied to the IV site,  $Z$  significantly decreases with increasing frequency because the current is strong enough to penetrate cell membranes and flows in ECF and ICF.

### 3.3 Bioelectrical impedance as a function of time before and after infiltration

Fig. 5 shows the change in impedance as a function of time when infiltration occurs during IV infusion into the vein. BI (before infiltration) represents when the IV solutions are properly infused. When infiltration occurred, the impedance gradually decreased because IV solution was accumulated in ECF of subcutaneous tissues. The gradual decrease in impedance with time after infiltration is

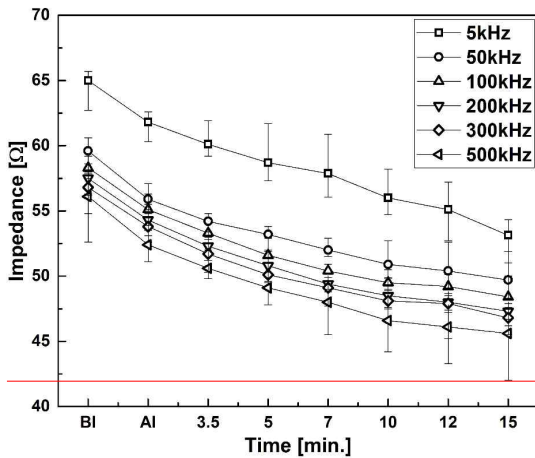


Fig. 5. Bioelectrical impedance as a function of time before and after infiltration.

clearly distinguished from figure 3, where the impedance was constant over time.

When a current of 5 kHz ( $2.1 \times 10^{-11}$  eV) was applied to the IV site, impedance was relatively large ( $\sim 65 \Omega$ ) because current flowed only in ECF. At 5 kHz, the decreasing impedance over time reflected accumulation of IV solution in subcutaneous tissue during infiltration. This phenomenon has been observed in impedance studies done by other researchers as well. Nescolarde et al. measured the impedance at 50 kHz in calf muscle before and after injury of football players, and confirmed that resistance for the more severe injured muscle was further reduced (11.9% in grade 1, 20.6% in grade 2, 23.1% grade 3) compared to the non-injured muscle ( $68 \Omega$ ). Their findings indicated that decreases in R reflected localized accumulation of fluid [24]. Thus, the decreasing impedance (Z) at AI (at infiltration) can be interpreted as infiltration, and gradually decreasing Z over time can be considered as gradual accumulation of IV solution and blood components leaking out from the vein into surrounding tissue. On the other hand, when a current with a frequency higher than 50 kHz ( $2.1 \times 10^{-10}$  eV) was applied to the IV site, the applied AC was strong enough to penetrate the cell membrane and flowed in ICF as well as ECF.

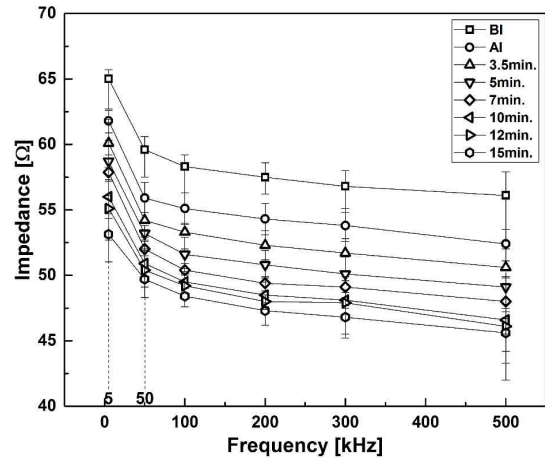


Fig. 6. Bioelectrical impedance as a function of frequency before and after infiltration.

### 3.4 Bioelectrical impedance as a function of frequency before and after infiltration.

Fig. 6 shows the change in impedance as a function of frequency when infiltration occurs. After infiltration, IV solution leaked from the vein acts as a variable resistor in ECF of the equivalent circuit as shown in fig.1. It was reported that hydrostatic disturbances, peripheral edema and the use of diuretic medication could affect the validity of BIA measurements in older age groups [25]. When a current having a frequency of 5 kHz ( $2.1 \times 10^{-11}$  eV) was applied to the IV site, impedance was significantly large because the current only flowed in ECF. However, the impedance decreased quantitatively over time, reflecting the accumulation of IV solution in ECF after infiltration. On the other hand, when a current having a frequency higher than 50 kHz ( $2.1 \times 10^{-10}$  eV) was applied to the IV site, impedance decreased gradually because the applied AC was strong enough to penetrate the cell membrane and flowed in ECF and ICF.

### 3.5 Infiltration and Discussion

Infiltrations are difficult to detect, especially at an early stage of infiltration. To date, the techniques to detect the infiltrations primarily relied on

clinical methods, which include visual and tactile examination of the skin and tissue surrounding the IV injection site for factors such as tissue pressure, color, edema, turgor and temperature [8]. Therefore, the visual and tactile examination technique is ineffective in detecting infiltration since tissue damage has already occurred when infiltration is checked. Researches on the prevention of infiltration have been recently performed to develop an IV infiltration management program to educate nurses participating in IV injection [26]. As a result of IV infiltration management program for pediatric patients receiving peripheral IV infusion, the occurrence of IV infiltration was reduced to less than 1%, which was significantly lower than control group. A safety event response team at Cincinnati Children's Hospital Center reduced peripheral intravenous (PIV) infiltration and extravasation. Improvement activities included development of a touch-look-compare method for hourly PIV site assessment, staff education and mandatory demonstration of PIV site assessment, and performance monitoring and sharing of compliance results [27]. Additionally, infiltration detection systems that use infrared light as light source are currently being developed. Infiltration has been recognized to decrease the reflectivity due to the leaked solution when comparing the reflectance of the lights before and after infiltration [11, 12]. However, these data do not accurately reflect accumulation of solution/fluid from the vein in skin and subcutaneous tissue because they are dependent on the partial reflectivity of IV solution exposed to the skin and infiltrated into subcutaneous tissue.

In this study, BIA was used to investigate the pathophysiological properties of biological tissues to detect infiltration. When IV solution was properly infused into the vein, there were no apparent changes in impedance over time. However, when infiltration occurred, impedance gradually decreased as a function of time, with some fluctuations. Using

multi-frequency bioelectrical impedance spectroscopy and an equivalent circuit model of human cell, IV solution leaking from the vein after infiltration was found to accumulate in ECF of surrounding skin and subcutaneous tissue, proposing an indicator for early detection of infiltration.

#### 4. CONCLUSION

In this study, bioelectrical impedance measurement was performed to detect the IV infiltration at an early stage. During infusion of IV solution at the rate of 60 ggt/min., impedance showed no significant changes (with some fluctuations) over time but decreased with frequency. Before and after the infiltration, impedance was measured as a function of time and frequency using bioelectrical impedance spectroscopy. When infiltration occurred, the bioelectrical impedance gradually decreased over time (proportional to amount of injection solution), with some variations. Using multi-frequency impedance spectroscopy and an equivalent circuit model of human cell, the IV solution leaking from the vein was found to accumulate in ECF of surrounding skin and subcutaneous tissues. Accordingly, it is suspected that infiltration may have occurred if impedance continues to decrease over time during IV infusion.

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