Early Detection of Infiltration Induced in the Veins of Pig’s Ear and Human’s Forearm By Using Bioimpedance: Pilot Study

Kim Jaehyung*, Hwang Youngjun**, Kim Gunho***, Jeong Ihn Sook****, Jeon Gyerok*****

ABSTRACT

An early detection of intravenous (IV) infiltration is essential to minimize the injuries during infusion therapy, which is one of the most important tasks for nurses in nursing settings. We report that bioelectrical impedance analysis is useful in the early detection of infiltration at puncture sites. When infiltration was intentionally induced in the vein of a pig’s posterior ear, impedance parameters \( R, X_C \) showed significant differences before and after infiltration. In particular, the relative resistance \( (R/R_0) \) decreased significantly at infiltration and then slowly decreased. This indicates that the vein in pig’s ear is thin and the amount of surrounding subcutaneous tissue, and hence the infiltrated solution accumulates slowly after infiltration. However, when infiltration was induced in the vein of human’s forearm, the relative resistance at 20 kHz decreased gradually over time. In the \( R-X_C \) graph, the positions in the case of infiltration induced in the pig’s ear shifted rapidly before and after infiltration, whereas the positions in the case of infiltration induced in the human’s forearm moved gradually during infiltration. Our findings suggest that the impedance parameters \( (R, R/R_0, X_C, R \) vs. \( X_C \) and \( C_m \)) are effective indicators to detect the infiltration early in a non-invasive and quantitative manners.

Key words: Intravenous (IV) Infiltration, Early Infiltration Detection, Multi-frequency Bioelectrical Impedance Analysis, Equivalent Circuit of Cell membrane.

1. INTRODUCTION

Infiltration is one of the most common health complications in infusion therapy during which unintended leakage of an IV solution into the surrounding subcutaneous tissue can occur [1]. The national standard practice of the Infusion Nurses Society (INS) requires that nurses administering IV medications or fluids should be aware of side effects and appropriate interventions prior to commencement of infusion [2]. Serious complications arise from the inadvertent administration of solutions or medications to tissues surrounding the IV catheter. When the agent is a non-preservative or drug, it is called infiltration, whereas when the agent is a vesicant medication, it is called extravasation. Both infiltration and extravasation can all have detrimental consequences, and pa-

* Corresponding Author: Gyerok Jeon, Address: 60612 Beomeo-ri, Mulgum-eup, Yangsan-si, Gyeongsangnam-do, Korea, TEL: +82-55-940-5548, FAX: +82-55-940-5083, E-mail: grjeon@pusan.ac.kr
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Research Institute of Nursing Science, Pusan National University (E-mail: jjkim@injae.ac.kr)

** Medical Science, School of Medicine, Pusan National University (E-mail: dudwna719@naver.com)
*** Medical Science, School of Medicine, Pusan National University (E-mail: kgh0383@naver.com)
**** College of Nursing, Pusan National University (E-mail: jeongis@pusan.ac.kr)
***** Dept. of Biomedical Engineering, School of Medicine, Pusan National University (E-mail: gjieon@pusan.ac.kr)

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patients may be severely injured by surgical intervention, limited functional experience, or even require amputation. The nurse can play vital role in reducing the risk of infiltration and extravasation through knowledge and skills in cannulation and the intravenous administration of drugs. Nurses should also be aware of early signs and symptoms of infiltration and extravasation and should be able to limit tissue damage promptly and effectively [3]. The most common complications in frequency order were forearm, hand, wrist, and frontal bone. Women and older patients are more vulnerable to these complications [4]. The use of appropriate tools for IV assessment can identify infiltration at early stages, thus reducing the possibility of more serious complications [5]. The INS devised a scale to assess the various signs and symptoms such as local edema, skin blanching, cooling of skin, pain, and numbness [6]. Despite the growing frequency of intravenous (IV) injections, establishing peripheral IV access is challenging, especially in patients with small or collapsed veins [7]. Infiltration can be caused by improper placement or dislocation of the catheter. Movement of the patient can cause the catheter to slip or through the vein [8]. The first sign may be that the drug fails to have the expected effect. Patients usually complain of immediate severe discomfort distal to the site of injection. Pallor, paraesthesia, hyperaemia, and cyanosis of the affected limb develop and severe cases may progress to develop profound oedema and gangrene [9]. Infiltration events are graded from 1 to 4, with higher number corresponding to greater severity [2].

Studies to detect infiltration in peripheral vein therapy have been performed using optical and electrical methods as early detection of infiltration helps to prevent the occurrence of serious injuries. An optical method that employs fiber optics and algorithms for tissue optics has been developed to facilitate non-invasive monitoring of IV sites [10, 11]. The tissue surrounding the injection site is exposed to a single wavelength of electromagnetic radiation (visible or infrared light), and the diffused light is collected by optical detector. Reflection, scattering, diffusion or relative intensity changes of emitted light provide a means of monitoring infiltration. These provide routine, automated, continuous and real-time monitoring for patients receiving IV therapy [11]. An early detection system (for example, IV watch Model 400) of peripheral IV infiltration and extravasation events through continuous monitoring of IV sites has been developed using near-infrared (NIR) light [12, 13]. In addition, researchers have attempted to use ultrasound to examine the exogenous fluids injected into cutaneous and subcutaneous tissues. Ultrasound could detect small volumes of fluids, such as cosmetic fillers and subcutaneous injections. Therefore, ultrasound could be a potential reference standard for the future evaluation of IV infusion monitoring devices [14]. However, an early infiltration detection system should be simple, reliable, economical, and capable of monitoring IV infiltration in a non-invasive manner for easy use in nursing and medical practice. Thus, the infiltration detection system using bioelectrical impedance analysis (BIA) satisfies these conditions because BIA is a safe, practical, and non-invasive method for measuring the biological tissues and materials [15]. Nowadays, BIA has been employed to diagnose diseases [16] and to assess the hydration status, body composition, muscle-fat ratio, obesity degree, lean balance, edema, and nutritional status of the patients [17, 18].

In this study, infiltration was induced by puncturing the vein with a needle in a pig's posterior ear. During infiltration, the IV solution and blood components accumulating in the subcutaneous tissues were investigated using impedance parameters such as resistance, relative resistance, reactance, and resistance vs. reactance, capacitance [19]. The impedance parameters showed significant differences in the vein in pig's posterior ear, but
they gradually changed in the vein in human’s forearm. The mechanism of infiltration induced in the veins of the pig’s posterior ear and the human’s forearm was quantitatively described using an equivalent circuit and impedance analysis, revealing that BIA could be applicable to the early detection of infiltration.

2. THEORY

2.1 Theory of Bioelectrical Impedance (Z)

Impedance (Z) is the opposition to the flow of an alternating current (AC) and, hence, depends on the frequency of the applied AC. Z is defined in terms of impedance magnitude (|Z|) and phase angle (θ) as shown in Eqs. (1)-(3) and Fig. 1. Impedance is a complex quantity consisting of resistance (R) of the total body water and reactance (Xc) due to the capacitance of the cell membrane [20]:

\[ Z = R + jX_c \]  
\[ |Z| = \sqrt{R^2 + X_c^2} \]  
\[ \theta = \tan^{-1}\left(\frac{X_c}{R}\right) \]  

The resistance of an object is determined by a shape and the material of the object. For a given shape, the resistance depends on the material the object is made from. In other words, different materials provide different resistances to the flow of electric charges. The resistance (R) of an object is directly proportional to the resistivity (ρ) of a material. The resistivity (ρ) is an intrinsic property of a material, and does not depend on its shape or size. The resistance (R) of an object of length L, made of a material having cross-sectional area A and resistivity ρ, is as follows [16].

\[ R(\omega) = \rho(\mu_m) \frac{L[m]}{A[m^2]} \]  

(4)

The capacitor affects the current, and has the ability to stop the current in a fully charged state. Since an AC voltage is applied, the root mean square (RMS) current is limited by the capacitor. Since the RMS current is regarded as the effective resistance of the capacitor for AC, RMS current I in a circuit containing only capacitor C is given by another version of the Ohm’s law as follows:

\[ I = \frac{V}{X_c} \]  

(5)

where V is the RMS voltage.

Reactance (Xc) of an object as shown in Eq. (6) is defined as resistance to voltage variation across the object and is inversely related with signal frequency (f) and capacitance (C) [21]. In biological systems, resistance is caused by total water across the body, and reactance occurs due to the capacitance of the cell membrane [16].

\[ X_c[f] = \frac{1}{2\pi fC[Frad]} \]  

(6)

where Xc, expressed in ohms, is called the capacitive reactance because the capacitor reacts in such a way as to impede the current. Xc is inversely proportional to the capacitance C. The larger the capacitance, the more charge the capacitor can store, and more current can flow. Capacitance is also inversely proportional to the frequency f; the greater the frequency, the less time there is to fully charge the capacitor, and hence it impedes current less [21].
2.2 Equivalent Circuit of ECF, ICF, and Cell Membrane

A basic understanding of normal body fluid physiology is required to appreciate the nuances of fluid therapy. Total body water (TBW) is distributed between the intracellular fluid (ICF) compartment (approximately 66%) and the extracellular (ECF) compartment (approximately 33%). ECF and ICF contain several ion types with different concentrations; the main ions are Na⁺ and Cl⁻ in ECF and are K⁺ and PO₄³⁻ in ICF [22]. These two spaces (ECF and ICF) are separated by cell membranes. The ECF compartment is further subdivided into intravascular (8% TBW) and interstitial (23% TBW) spaces [23], and these compartments are separated by the capillary wall. The cell membranes between the fluid compartments have different permeability to different solutes based on size, charge, and conformation. An equivalent electrical circuit model has been used to investigate the response of different tissue components to AC having multi-frequency. Our model considers seven electrical components: skin resistance, contact capacitance, fat resistance, fat capacitance, extracellular resistance, intracellular resistance, and cell membrane capacitance [24]. The human body model consists of resistances (Rₑ, Rₘ, Rᵢ) and capacitance (Cₘ) connected in parallel or 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. Cells constituting human organs consist of ECF and ICF that behave as electrical conductors whereas the cell membrane acts as a resistor and capacitor [25, 26]. Fig. 2 shows the equivalent circuit of a cell in the human body. Table 1 lists the descriptions of symbols represented in Fig. 2.

Since the resistance (Rₘ) and the capacitance (Cₘ) of cell membrane are connected in parallel, the reactance (Xₑ) of the cell membrane in Fig. 2 can be expressed as follows:

\[
Xₑ = \frac{1}{\frac{1}{Rₘ} + juCₘ} = \frac{Rₘ}{1 + juRₘCₘ}
\] (7)

The reactance (Xₑ) of the cell membrane and the resistance (Rᵢ) of the ICF connected in series can be expressed as (8).

\[
Zᵢ(ju) = Rᵢ + Xₑ = Rᵢ + \frac{Rₘ}{1 + juRₘCₘ}
\] (8)

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
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<tbody>
<tr>
<td>Cₘ</td>
<td>Capacitance of cell membrane</td>
</tr>
<tr>
<td>Rₘ</td>
<td>Resistance of cell membrane</td>
</tr>
<tr>
<td>Rᵢ</td>
<td>Resistance of ICF</td>
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<tr>
<td>Xₑ</td>
<td>Reactance of cell membrane</td>
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<tr>
<td>Zᵢ</td>
<td>Impedance of Xₑ and Rᵢ</td>
</tr>
<tr>
<td>Z</td>
<td>Impedance of Zᵢ and Rᵢ</td>
</tr>
<tr>
<td>I</td>
<td>Current through both ECF and ICF</td>
</tr>
<tr>
<td>Iᵢ</td>
<td>Current through only ECF</td>
</tr>
<tr>
<td>Iₑ</td>
<td>Current through both cell membrane and ECF</td>
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Fig. 2. Human body composed of resistors (Rₑ, Rᵢ, Rᵢ) and capacitor (Cₑ) connected in parallel or 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.
\[ Z = \frac{1}{\frac{1}{R_e} + \frac{1}{R_i}} = \frac{R_i Z_i}{R_i + Z_i} \]  \hspace{1cm} (9)

The reactance \((X_C)\) of the cell membrane depends on the applied frequency. When the frequency of the applied AC is low, \(X_C\) and \(Z_i\) increase in Eqs. (7) and (8), so that \(Z\) increases. When the frequency of the applied AC is high, the opposite phenomenon occurs and then \(Z\) decreases.

3. METHOD

3.1 Intravenous infusion and induced infiltration in the vein of pig’s posterior ear

Electrodes for applying the current and collecting the voltage were attached to both sides of the IV infusion site. Ag/AgCl electrode (2223H, 3M, Korea) with foam tape and sticky gel was used to minimize the interfacial effects between the electrode and the skin. Ag/AgCl electrode is now used in most bioimpedance measurements because it has a well-defined DC potential with electrolyte gel to minimize the gap impedance between skin and electrodes. Circular and rectangular electrode shapes with a contact area greater than 4 cm² are the most commonly used shapes [27]. After inserting the PIV catheter into a vein of a pig’s posterior ear, impedance parameters \((R, R/R_{Bi}, X_C, R \text{ vs. } X_C, C_m)\) were measured as a function of time and frequency while infusing an IV solution at the rate of 4 gtt. (4 drops per min.) to prevent blood clotting. Then, the infiltration was intentionally induced by pushing the needle through the vein wall into the subcutaneous tissue in a pig’s posterior ear as shown in Fig. 3(a). Fig. 3(b) shows the impedance measurement in human’s forearm while infusing IV solution at the rate of 60 gtt. (60 drops per min.) [28]. Impedance parameters were measured using multi-channel impedance measuring instrument (Vector Impedance Meter) developed by Kim et al. [29]. AC with 7 different frequencies ranging from 20–500 kHz was applied to the electrodes. This study on animals was approved by the Pusan National University Yangsan Hospital Animal Care and Use Committee (PNUYH-2017-040).

4. RESULTS AND DISCUSSIONS

4.1 Resistance \((R)\) as a function of time \((t)\)

Fig. 4 shows the resistance \((R)\) as a function of time and frequency before and after infiltration while infusing the IV solution into the vein of pig’s ear. An AC was applied to the electrodes attached to both sides of IV infusion site and the applied frequency was varied. After infiltration began to occur (AI), the resistance decreased significantly and then decreased slowly. When AC having a frequency of 20 kHz was applied to the infiltration

![Image](a)

Fig. 3. (a) Electrodes attached to a pig’s posterior ear for detecting the infiltration, (b) Circular electrodes used to measure the impedance to detect vein–induced infiltration into the human’s forearm, Outside band electrodes are used for detecting infiltration with another measuring device.

![Image](b)

Fig. 4. Resistance as a function of time during infusing IV solution into the vein in a pig’s ear.
site, the resistance decreased significantly before and after infiltration. Since AC having a frequency of 20 kHz could not pass through the cell membranes, a sharp reduction in resistance during infiltration indicates that a considerable amount of the IV solution flowing out of the vein is accumulating in the ECF including the interstitial fluid (ISF). A subsequently gradual decrease in the resistance over time reflects that the IV solution is still accumulating in the surrounding subcutaneous tissues. In contrast, in previously reported study [30] on the infiltration induced in the human’s forearm, the resistance decreased gradually over time because the IV solution leaking out of a vein in the human’s forearm continued to accumulate gradually in the surrounding thick subcutaneous tissue after infiltration.

4.2 Relative resistance ($R/R_0$) as a function of time ($t$)

Fig. 5 shows the relative resistance (white squares) measured at 20 kHz in the veins of a pig’s posterior ear as a function of time. Compared to the relative resistance before infiltration (BI), the relative resistance significantly decreased at infiltration (AI) and then slowly decreased thereafter. This indicates that the vein in the pig’s ear was thin so that the infiltrated IV solution accumulated slowly after infiltration. In contrast, the right hand side in Fig. 5 also shows the relative resistance (dark squares) measured at 20 kHz in the human forearm as a function of time. The relative resistance gradually decreased over time. This indicates that the vein in the human’s forearm is large and there are large amount of surrounding subcutaneous tissues, so that the IV solution continue to accumulate in subcutaneous tissues over time. According to our previous paper [28] on the infiltration induced in the human’s forearm, the relative impedance was found to gradually decrease with time. The thin and weak venous blood vessels of the newborns or infants are expected to exhibit infiltration and impedance behaviors different from those of adult’s forearms with thick blood vessels and surrounding subcutaneous tissues.

4.3 Reactance ($X_C$) as a function of time ($t$)

Fig. 6 shows the reactance ($X_C$) of the cell membranes as a function of time and frequency while infusing the IV solution into the vein in the pig’s ear. The magnitude of the reactance largely decreased at infiltration (AI) and then very slowly decreased. This is because the infiltrated IV solution and blood components are adsorbed on the cell membranes, which in turn reduces the ability

![Fig. 5. Relative resistance ($R/R_0$) measured at 20 kHz in the pig’s ear and human’s forearm as a function of time.](image)

![Fig. 6. Reactance as a function of time during IV solution infusion into the vein of pig’s ear.](image)
tissues to slow the current flowing through the cell membrane. The magnitude of the reactance decreases most remarkably at 20 kHz, so this can be used as an indicator to detect infiltration.

4.4 Resistance ($R$) versus reactance ($X_C$)

Fig. 7 shows the relationship between resistance ($R$) and reactance ($X_C$) monitored at 20 kHz during the infusion of the IV solution into the veins in pig’s ear and human’s forearm. When infiltration was induced in the vein of the pig’s ear, the position (white squares) shifted to lower left in the $R$-$X_C$ graph. This suggests that when the infiltration occurs, the IV solution and blood components accumulate in the subcutaneous tissues of pig’s ear and then accumulate in the subcutaneous tissues after infiltration. On the other hand, when infiltration was induced in the vein of human’s forearm, the position (black squares) gradually changed to the lower left in $R$-$X_C$ graph, revealing that the IV solution and blood components leaking out of the vein continue to accumulate in the surrounding subcutaneous tissues [31].

4.5 Capacitance ($C_m$) as a function of time ($t$)

Fig. 8 shows the capacitance ($C_m$) of the cell membrane as a function of time while infusing the IV solution into the vein in the pig’s ear. The capacitance of the cell membrane significantly increased at infiltration (AI) and then gradually increased. This is because the IV solution and blood components leaking out of the vein during infiltration are adsorbed on the cell membrane in the subcutaneous tissue, hence reducing the ability of the cell membrane to temporarily regulate the electric current. The capacitance of the cell membrane was prominently increased at 20 kHz, which can be used as an indicator for detecting infiltration.

4.6 DISCUSSION

Infiltration is generally known to be difficult to detect at an early stage. To date, the techniques of detecting the infiltration depend primarily on clinical methods, which include visual and tactile examination of the skin and subcutaneous tissues surrounding the IV injection site for factors such as tissue pressure, color, edema, swelling and temperature [9]. However, these methods have serious problems in detecting infiltration because infiltration is better identified after the tissue damage has already occurred in the subcutaneous tissue. In ad-
dition, the existing infiltration detection systems have been mainly developed using infrared light. Infiltration was identified by comparing the high reflectance of light before infiltration and low reflectance of light due to the leaking solution after infiltration [12, 32]. However, these data does not accurately reflect the accumulation of solution/ fluid from the vein into surrounding subcutaneous tissue, since they rely on the partial reflectivity of the IV solution exposed to the skin and the infiltrated IV solution (also blood components).

In this study, the impedance parameters ($R, R/R_{bl}, X_C, R$ vs. $X_C$ and $C_m$) and the equivalent circuit model of the cell were utilized to effectively investigate the infiltration induced in the veins of pig’s ear and human’s forearm as a function of time and frequency. When the infiltration was intentionally induced in the vein of pig’s ear, the impedance parameters showed significant differences before and after infiltration. They were able to quantitatively distinguish infiltration in seven frequency ranges (20–500 kHz). Impedance parameter values from 20 kHz reflected the IV solution accumulated in ECF during infiltration. Using bioelectrical impedance parameters and an equivalent circuit model of the cells, the IV solution and blood components leaking out of the vein after infiltration were confirmed to accumulate in the ECF, suggesting the impedance parameters as an indicator for early detection of infiltration. The impedance method used in this study is simple, non-invasive and economical, and the reliability of the experiment to detect infiltration is clearly validated. Thus, this technique can be extended to nurses in the nursing site to confirm the infiltration for point of care. In order to develop infiltration detection device for point of care, our research team is currently conducting research on infiltration using impedance parameters for patients in a long term care hospital. In the case of modifying the electrode module to reduce the measuring time and to allow continuous measurement, it is also possible to detect the early infiltration using the automated impedance device.

5. CONCLUSION

In this study, the impedance parameters were measured as a function of time and frequency while infusing the IV solution into the veins of a pig’s posterior ear and the human’s forearm. Experimental results are summarized as follows. First, when infiltration was intentionally induced in the vein of pig’s ear, impedance parameters ($R, X_C$ and $C_m$) exhibited significant differences before and after infiltration. However, when infiltration was induced in the vein of the human’s forearm, impedance parameters gradually changed because the IV solution accumulates in thick subcutaneous tissue. Second, the relative resistance ($R/R_{bl}$) at 20 kHz largely decreased with infiltration (AI), and slowly decreased thereafter. But, when infiltration was intentionally induced in the vein of the human’s forearm, the relative resistance at 20 kHz gradually decreased over time. This indicates that the vein in the human’s forearm is thick and there are many subcutaneous tissues, so that the IV solution continue to accumulate in subcutaneous tissues over time. Third, when infiltration was induced in the vein of pig’s ear, the position (BI) rapidly shift lower left to the position (AI) in the $R-X_C$ graph. These indicates that pig’s posterior ear is thin and the surrounding subcutaneous tissues are so small that the IV solution and blood components largely accumulate in the subcutaneous tissues during infiltration and slightly accumulate after infiltration. However, when infiltration was induced in vein of human’s forearm, the position gradually moved over time in the $R-X_C$ graph, revealing that the IV solution and blood components leaking out of the vein continue to accumulate in the surrounding subcutaneous tissue. Our findings suggest that it may be applicable to infiltration detection in neonates or infants with thin veins or in severe and elderly patients with frequent infiltration.
REFERENCE


Kim Jaehyung
He received B.S. and M. S. degree from Pusan National University, Korea, in 1979 and 1981, respectively, and Ph. D degree from Kyungnam University, Korea, in 1992. He was visiting scientist at Liquid Crystal Institute of Kent State University, USA in 1993, and visiting professor at Physics Department of Portland State University, USA, in 2003. He is currently researcher at Research Institute of Nursing Science, Pusan National University and has deep interest in bio-electrical impedance, electro-dermal activity, and electrical stimulator, etc.

Hwang Youngjun
He received a bachelor’s degree from Pusan National University, Korea, 2017. He is in the master’s degree in dept. of medical science, Pusan National University, Yangsan, Korea.

Kim Gunho
He received a bachelor’s degree from Pusan National University, Korea, 2017. He is in the master’s degree in dept. of medical science, Pusan National University, Yangsan, Korea.

Jeong Ihn Sook
She is a professor of College of Nursing, Pusan National University. She graduated College of Nursing, Seoul National University. Her subject area is Nursing, Pharmacology, Toxicology and Pharmaceutics, Immunology and Microbiology, Research ethics, and Early detection of IV infiltration

Jeon Gye-Rok
He received B.S. and M.S. degree from Busan national university, Korea, 1978 and 1982, respectively. And doctor degree from Donga University Korea, 1993. He is currently professor, department of biomedical engineering, school of medicine, Busan national university, and working at Busan national university Yangsan hospital. His major is biomedical signal processing and biomedical measurement system.