Journal of information and communication convergence engineering
http://jicce.org

J. Inf. Commun. Converg. Eng. 15(2): 123-130, Jun. 2017 Regular paper

Early Detection of Intravenous Infiltration Using Multi-frequency Bioelectrical Impedance Measurement System: Pilot Study

Jaehyung Kim[1], Beumjoo Shin[2], and Gyerok Jeon[3*], *Member, KIICE*

[1]Research Institute of Nursing Science, Pusan National University, Yangsan 50612, Korea
[2]Applied IT and Engineering, Pusan National University, Milyang 50463, Korea
[3]Department of Biomedical Engineering, Pusan National University School of Medicine, Yangsan 50612, Korea

Abstract

The early detection of intravenous (IV) infiltration is necessary to minimize the injury caused by the infiltration, which is one of the most important tasks for nurses. For detecting early infiltration in patients receiving invasive vein treatment, bioelectrical impedance was measured using multi-frequency bioelectrical impedance. The impedance decreased significantly at infiltration, and then decreased gradually over time after infiltration. The relative impedance at 20 kHz decreased remarkably at infiltration, and then gradually decreased thereafter. In addition, the impedance ratio increased temporarily at infiltration and then gradually decreased over time. Furthermore, the impedance at each frequency decreased quantitatively over time. This indicates that IV solution leaking from the vein due to infiltration accumulates in the subcutaneous tissues. Moreover, slopes of log Z vs. log f differently decreased with increasing log f, indicating that the impedance exhibits different responses depending on the frequency.

Index Terms: Early detection, Impedance, Impedance ratio, Infiltration, Multi-frequency impedance, Relative impedance

I. INTRODUCTION

Placement of an intravenous (IV) catheter for administration of parenteral therapy is one of the most common invasive procedures performed in hospitals [1]. The millions of peripheral intravenous (PIV) catheters used each year are recommended for 72–96 hour replacement in adults. This routine replacement increases health-care costs and staff workload and requires patients to undergo repeated invasive procedures [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 extravasation refers to the accumulation or diffusion of effervescent fluid or drug [4]. Infiltration occurs when a catheter tip inserted into a peripheral vein penetrates through a weak vessel wall and the fluid infused through IV is leaked to the surrounding tissues [5]. Extravasation occurs when the osmotic pressure of injected fluid is high or the blood vessel walls and surrounding tissues are damaged due to pharmacological factors of the fluid [6].

Studies on infiltration have been carried out by many

Received 06 January 2017, **Revised** 24 January 2017, **Accepted** 03 May 2017
***Corresponding Author** Gyerok Jeon (E-mail: grjeon@pusan.ac.kr, Tel: +82-55-360-1927)
Department of Biomedical Engineering, Pusan National University School of Medicine, 49 Busandaehak-ro, Mulgeum-eup, Yangsan 50612, Korea.

Open Access http://doi.org/10.6109/jicce.2017.15.2.123 print ISSN: 2234-8255 online ISSN: 2234-8883

other researchers in various ways [7, 8]. Thigpen presented an initial approach to nursing care for PIV infiltrations to guide clinicians based on clinical experience, descriptive studies, and reports from expert committees [7]. These 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 IV tube for blood return, and visual and tactile examination of the skin and tissues surrounding IV injection site for factors such as tissue pressure, color, edema, turgor and temperature [8]. Ultrasound guidance reduced the number of attempts, the number of needle redirections, and the overall time to catheter placement. In a sample of pediatric emergency department patients with difficult access, ultrasound-guided intravenous cannulation required less overall time, fewer attempts, and fewer needle redirections than traditional approaches [9].

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 PIV treatment have been performed using a variety of technologies including temperature, ultrasound, microwave, near-infrared, and impedance measurement [10]. An IV infiltration detection apparatus coupled with optic fibers and optic module (consisting of LED and photo diode) have also proposed to monitor intravenous failure [11]. Peripheral IV system (ivWatch Model 400; ivWatch, Hampton, VA, USA) using the visual and near-infrared light ($\lambda = 660, 735, 850, 960$ nm) was developed to monitor the IV infusion site for infiltration [12]. 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.

To solve the 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 [13-15]. BIA relies on the conduction of radiofrequency electrical current by the fluid (water, interstitial fluid, and plasma), electrolytes, and permeability of cell membrane in the tissue [16]. Furthermore, BIA 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 patients [17, 18].

In this study, bioelectrical impedance (BI) parameters were measured as a function of time during infusing IV solution into the vein. In order to determine the effect of IV solution accumulated in the skin and subcutaneous tissues surrounding IV site, BI was measured as a function of time before and after infiltration. When IV solution penetrated into the surrounding tissues during and after the infiltration, the changes of BI parameters were also observed according to the frequency applied to the cell membrane.

II. SYSTEM MODEL AND METHODS

A. Characteristics of BI

Impedance of the human body is a major factor affecting the intensity of the current flowing through the human body when the applied voltage is constant. Assuming that the human body is an electrical conductor, impedance values are measured differently depending on morphological structural characteristics of various components such as tissues and cells, moisture in the body, and blood constituting various organ systems. The impedance varies depending on the path of the current applied to the human body, the applied frequency, the cross-sectional area of the measurement site, and the structural characteristics.

Biological tissues consist of cell membranes, which are partial electrical insulator, and extracellular and intercellular fluid containing various electrolytes, ions, and interstitial fluid. In addition, they have unique electrical properties due to various differences such as cell arrangement and bone structure, and react differently according to the applied frequency. Since the electrical conductivity of the tissue and the cell is differently measured according to the frequency of the alternating current applied to the human body, the distribution of the human body component can be obtained by using impedance. In general, AC having a frequency ranging from 5 to 200 kHz is usually applied to measure BI. The 5 kHz alternating current does not pass through the cell membrane, so it is applied to the measurement of extracellular fluid. The 50 kHz alternating current can be seen as a critical frequency that begins to pass through the cell membrane. However, this frequency varies according to gender, age, nutrition, health status, etc. At 50 kHz, the ratio of the current flowing through the extracellular fluid and the current flowing through the cell membrane to the intracellular fluid (ICF) is about 8:2. The alternating current having 200 kHz is applied to the total body water (TBW) measurement because it flows well into the extracellular and ICFs. TBW occupies 60% of the body mass depending on sex, age, and obesity. The ICF accounts for about 40% of TBW and the extracellular fluid (ECF) about 20% of TBW. Furthermore, 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, while the cell membrane acts as a partial electrical insulator or capacitor [19].

The equivalent circuits for human cell models have been proposed in various ways [20, 21] in order to measure BI. In this study, the equivalent circuit presented in our previous research [22] was applied to investigate early infiltration. The energy applied to the cell membrane varies with the frequency applied to the human body, and a minimum energy (2.07×10^{-10} eV) should be applied for the AC current to pass through the cell membrane. The energy (E) required for the alternating current to pass through the cell membrane increases with increasing frequency (f): $E = hf$ (h= 6.625×10^{-34} J/s). When the alternating current applied to the human body is 50 kHz, the energy applied to the cell is 2.07×10^{-10} eV. Therefore, when a current having the frequency lower than 50 kHz is applied to human body, the reactance (X_C) and capacitance (C_m) of cell membrane becomes large and then, the current cannot pass through the cell membrane. On the other hand, when the frequency of alternating current is higher than 50 kHz, the reactance and capacitance of the cell membrane decreases, and then the current can pass through the cell membrane.

When the frequency of alternating current is between 100 and 200 kHz, the energy above the threshold (0.41 to $0.83 \times 10^{-9}\ eV$) that can pass through the cell membrane is applied to the human cell. Since the conductivity and permeability of the cell membrane are rapidly increased in proportional to frequency, the reactance (X_C) of the cell membrane is reduced and therefore the electrostatic capacitance (C_m) of cell membrane is also rapidly reduced. In this case, the applied AC flows not only outside the cell membrane (ECF) but also inside the cell (ECF).

B. Implementation of MF-BIMS

In this study, a multi-frequency bioelectrical impedance measurement system (MF-BIMS) developed by Kim et al. [23] was used to detect the infiltration. MF-BIMS applies weak alternating current (800 μA) and radiofrequency (RF) power of multi-frequencies (1 kHz to 2 MHz) to the human body through the electrodes and receives the lost RF power at the body's measurement site to measure impedance values (impedance, Z; resistance, R; reactance, X_C; and phase angle, θ).

C. Subject

Two healthy males were selected as subjects in order to conduct a small-scale exploratory clinical trials study led by researchers. The purpose and experimental contents of this study were explained to the subjects and their written consent was obtained. Subjects were 2 males with a mean age of 61.0 years (±2.0 years), an average height of 168.0 cm (±3.0 cm), an average mass of 68.0 kg (±3.0 kg), and an average body mass index of 24.23 kg/m^2 (±0.34 kg/m^2). 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 Institutional Review Board committee of Pusan National University Yangsan Hospital (IRB No. 03-2016-017).

D. Peripheral IV Infusion and Induced Infiltration

After inserting PIV catheter into the vein, a transparent dressing (10.2 cm×7.4 cm; Sewoon Medical, Cheonan, Korea) was attached to ensure the leakage of IV solution from vein due to infiltration with the naked eye. Ag/AgCl electrodes (2223H; 3M, St. Paul, MN, USA) used for ECG measurement were attached to both ends of transparent dressing mounted on the skin that IV solution is being infused as shown in Fig. 1. An electrode with an area of about 0.783 cm^2 was used to measure the voltage after applying AC to the IV infusion site.

BI was measured at eight different times up to 15 minutes while IV solution was being injected at a flow rate of 15 gtt. (15 drops/min or 1 mL/min) to the vein. In addition, an infiltration of isotonic solution was intentionally induced by pushing the needle through the venous wall in the left forearm into the subcutaneous tissue during measuring BI. Then, the transparent dressing was immediately mounted on IV site to visually observe swelling of the tissue around infiltrated site. AC having 8 different frequencies (20, 50, 100, 200, 300, 500, 700, and 1,000 kHz) was applied to IV site through two Ag/AgCl electrodes and the voltage between two electrodes was measured to obtain BI.

Fig. 1. Arrangement of electrodes to measure BI during infiltration (round electrodes in the middle). Outer band electrodes are used in a commercial impedance spectroscopy (MultiScan 5000, MultiScan Ltd, UK) for comparison experiment.

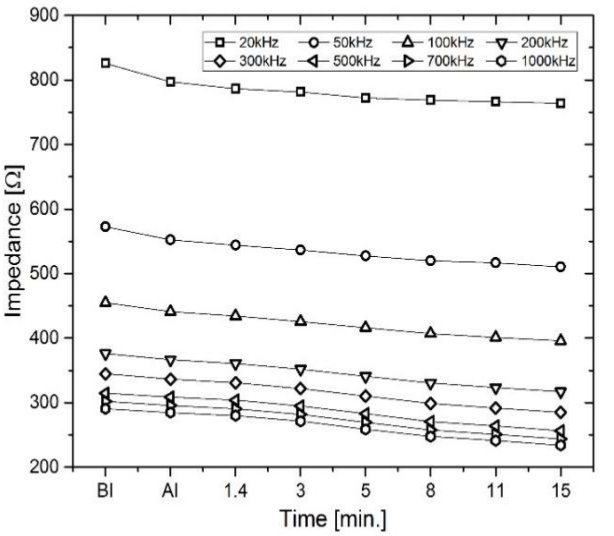

Fig. 2. Impedance (Z) as a function of time before and after infiltration. Z decreased significantly at AI and then gradually.

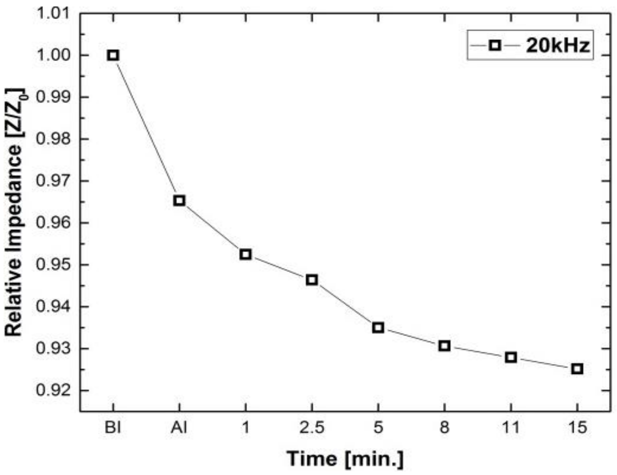

Fig. 3. Relative impedance (Z/Z_{BI}) at 20 kHz as a function of time. The relative impedance at 20 kHz decreased remarkably at infiltration and gradually decreased thereafter.

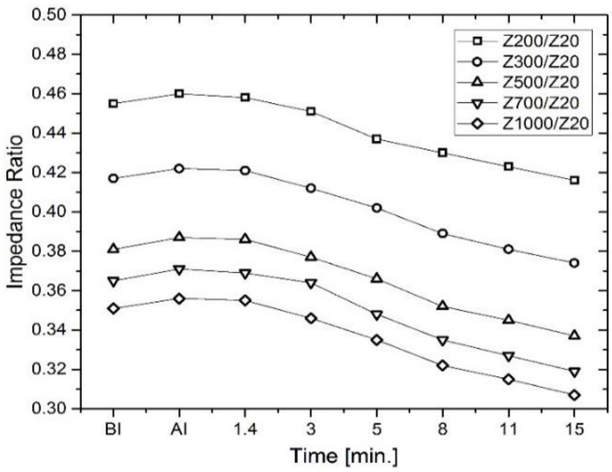

Fig. 4. Impedance ratio as a function of time. The impedance ratio increased temporarily at infiltration, and then gradually decreased.

III. RESULTS

A. Impedance (Z) as a Function of Time

Fig. 2 shows the measured impedance (Z) as a function of time and frequency before and after infiltration. An alternating current having eight different frequencies (20, 50, 100, 200, 300, 500, 700, and 1,000 kHz) was applied to IV site during infusing IV solution into the vein. BI (before infiltration) indicates the time that the IV solution is being infused into the vein properly. AI (at infiltration) represents the time at which IV solution was infiltrated during IV infusion.

Z decreased with increasing time and frequency. When infiltration occurred, Z decreased more significantly at low frequencies (20–200 kHz). Therafter, Z gradually decreased over time because IV solution and blood components penetrated into the surrounding skin and subcutaneous tissues. When AC having a frequency of 20 kHz (0.81×10^{-10} eV) was applied to IV site, Z was significantly large because the current primarily flowed into ECF. The decreasing Z at 20 kHz over time reflects IV solution being accumulated in the skin and subcutaneous tissue during infiltration [5]. On the other hand, when AC having a frequency higher than 50 kHz (2.07×10^{-10} eV) was applied to IV site, the applied AC was strong enough to penetrate the cell membrane and then flowed into ECF and ICF. Thus, the decreasing Z at AI can be considered as an infiltration. That is, the decreasing Z over time can be interpreted as a gradual accumulation of IV solution and blood compontnts leaking from the vein into surrounding subcutaneous tissues.

B. Relative Impedance (Z/Z_{BI}) as a Function of Time

Fig. 3 shows the relative impedance (Z/Z_{BI}) at 20 kHz as a function of time. The relative impedance indicates the ratio of the impedance measured at the infiltration and thereafter to the impedance measured at BI, which reveals the rate of change in impedance over time. In Fig. 2, AC having a frequency of 20 kHz mainly flowed in ECF, so decreasing Z/Z_{BI} over time reflected well IV solution being accumulated in ECF due to infiltration. At 20 kHz, the relative impedance decreased highly at infiltration and then decreased gradually. Thus, it is possible to detect early infiltration of IV solution into the vein by using the decreasing relative impedance over time.

C. Impedance Ratio as a Function of Time Before and After Infiltration

The impedance ratio is defined to the impedance (Z) measured at 200 kHz to that measured at 5 kHz, revealing a ratio of TBW/ECW fluid distribution [24]. The impedance spectroscopy (named Impedance Vector) in this study showed stable signal between 20 kHz and 1,000 kHz. Thus, the modified impedance ratio was obtained using the impedance at 200, 300, 500, 700, and 1,000 kHz to that at 20 kHz, respectively. Fig. 4 shows the impedance ratio as a function of time. The impedance ratio increased temporarily at infiltration, and then gradually decreased. Impedance ratio could be utilized to detect an early infiltration during infusing IV solution into the vein.

D. Impedance as a Function of Frequency during Infusing IV Solution

Fig. 5 shows impedance as a function of frequency during infusing IV solution into the vein. Impedance decreased nearly exponentially with increasing frequency. Impedance at each frequency decreased quantitatively with time. This indicates that IV solution leaking from the vein due to infiltration being accumulated in the surrounding skin and subcutaneous tissues. When the current having a frequency of 20 kHz (0.81×10^{-10} eV) was applied to IV site, the impedance was significantly large because the current mainly flowed in ECF, reflecting IV solution (also blood components) being accumulated in ECF due to infiltration. On the other hand, when AC having a frequency higher than 50 kHz (2.07×10^{-10} eV) was applied to IV site, the impedance was gradually decreased because the applied AC was enough to penetrate the cell membrane and flowed in ICF as well as ECF. These resultss are consistent with the other result reported by other researchers: hydrostatic disturbances, peripheral oedema and the use of diuretic medication could affect the validity of BIA measurements in older age groups [25].

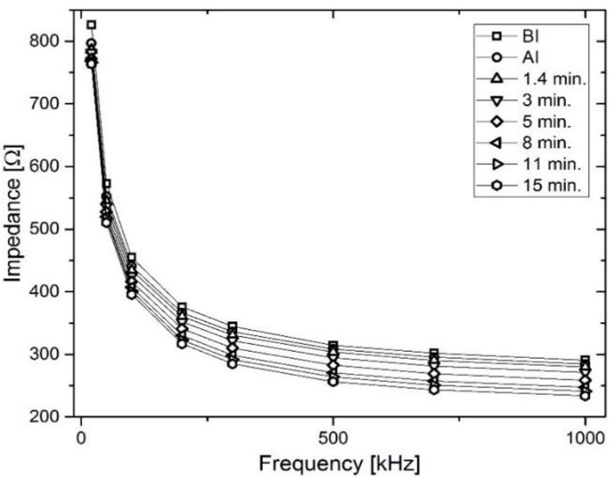

Fig. 5. Impedance as a function of frequency during infusing IV solution into the vein. Impedance at each frequency decreased quantitatively with time. This indicates that IV solution leaking from the vein due to infiltration accumulates in the surrounding skin and subcutaneous tissues.

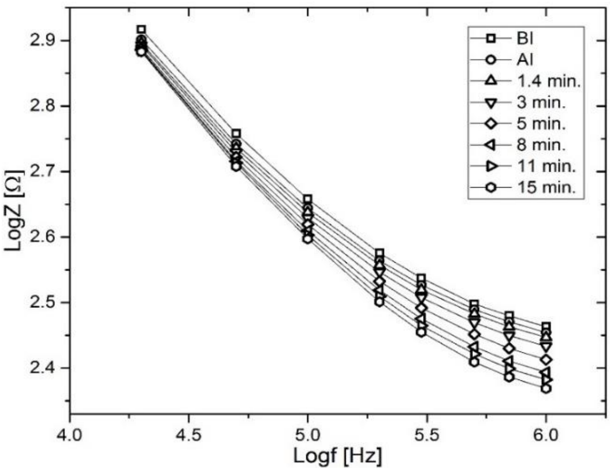

Fig. 6. Log Z as a function of Log f. The slopes of log Z vs. log f differently decrease with increasing log f. This indicates that impedance exhibits different responses depending on the frequency.

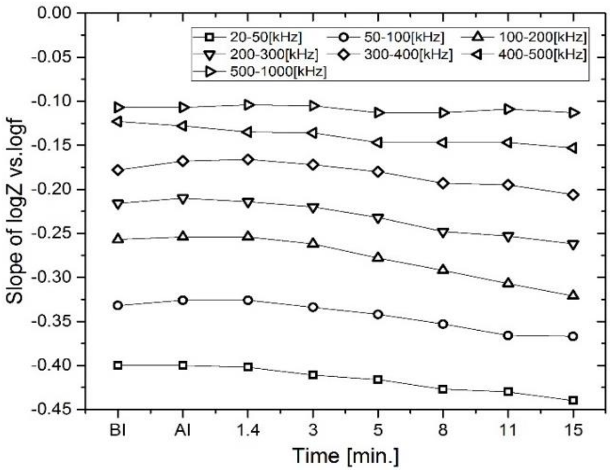

Fig. 7. Slopes of log Z vs. log f as a function of time. The magnitude of slope over time decreased slightly at AI and then gradually increased.

E. Log Z as a Function of Log f Before and After Infiltration

Fig. 6 shows log Z plot as a function of log f. The slopes of log Z vs. log f differently decrease with increasing log f. This indicates that impedance exhibits different responses depending on the frequency. At low frequencies below 50 kHz, the current primarily flows in ECF. However, as the frequency increases, the current flowing in ECF decreases while the current flowing in ICF gradually increases. In addition, the impedance decreased with time at each frequency.

F. Slopes of Log Z versus Log f Before and After Infiltration

Fig. 7 shows the slope of log Z versus log f as a function of time. The magnitude of slope was large when the frequency was low (between 20 and 50 kHz) and then decreased with increasing frequency. The magnitude of slope over time decreased at AI and then gradually increased. Slight increase in slope of log Z versus log f after infiltration was observed in the frequency ranges of 20–50 kHz, 100–200 kHz and 200–300 kHz, indicating IV solution being accumulated in ECF after infiltration.

IV. DISCUSSION AND CONCLUSION

IV infiltrations are difficult to detect, especially at an early stage of infiltration. To date, techniques for detecting infiltrations have relied primarily on clinical methods, which include visual and tactile examination of the skin and tissue surrounding IV injection site for factors such as tissue pressure, color, edema, turgor and temperature. However, when the nurses check infiltration by visual and tactile examination, the damage to the skin and subcutaneous tissues is already under way. Therefore, these methods are often used in nursing and medical practice, but are inefficient in detecting infiltration.

Researches on infiltration have been recently performed to develop an IV infiltration management program to educate nurses participating in IV injection therapy [26]. As a result of IV infiltration management program for pediatric patients receiving PIV infusion, the occurrence of IV infiltration was reduced to less than 1%, which was significantly lower than control group [27]. In addition, Safety Event Response Team at Cincinnati Children’s Hospital Center reported to reduce PIV infiltration and extravasation [28]. 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. Furthermore, infiltration detection systems using infrared light as light source have currently being developed. Infiltration has been recognized to decrease the reflectivity due to the leaked solution when comparing the reflectance of lights before and after infiltration. However, these data do not accurately reflect IV solution accumulating from the vein into the skin and subcutaneous tissues because they are dependent on the partial reflectivity of IV solution exposed to the skin and infiltrated into subcutaneous tissue [11, 12].

In this study, early infiltration was detected using BIA. Infiltration was intentionally induced by pushing the injection needle into the vein wall during infusing an isotonic IV solution into the vein. When infiltration occurred, the impedance decreased over time as IV solution accumulated in ECF (also interstitial fluid). These studies have been confirmed in a similar way by other researchers. Namely, localized impedance measurements could detect with very high sensitivity as little as 20 μL in ECF infused from a subcutaneously located catheter [29]. Thus, BI parameters (Z, Z/Z_{BI}, R_x/R_{20kHz}, Z vs. f, log Z vs. log f, and slop of log Z vs. log f) could be non-invasively used for early detection of infiltration phenomena with various side effects in nursing and medical practice.

In conclusion, BI measurement was performed to detect IV infiltration early in this study. During infusing IV solution at the rate of 60 gtt. (60 drops/min), impedance was measured as a function of time for frequencies ranging from 20 to 1,000 kHz. When infiltration occurred, impedance gradually decreased over time (proportional to the amount of infusing IV solution). Using impedance at 20 kHz and an equivalent circuit model, IV solution leaking from the vein was confirmed to be accumulated in ECF of skin and subcutaneous tissue. Accordingly, the gradual decreases in impedance over time during infusing IV solution into the vein can be treated as the occurrence of infiltration The following impedance parameters could effectively differentiate an early infiltration during IV infusion into the vein. First, impedance significantly decreased at infiltration and then gradually decreased. At 20 kHz, the relative impedance decreased highly at infiltration and then decreased gradually. Thus, it is possible to detect early infiltration of IV solution into the vein by using the decreasing relative impedance over time. Second, impedance ratios were the largest at infiltration and then gradually decreased. Third, log Z vs. log f indicated that impedance decreased differently depending on the frequency before and after infiltration. That is, the magnitude of slope of log Z vs. log f at infiltration increases at infiltration, and then gradually decreased in 20–400 kHz. These parameters reflect the accumulation of IV solution and blood from the vein into skin and subcutaneous tissue during IV infusion, proposing an early detection of infiltration.

In future studies, it is necessary to apply impedance parameters applied in this study by dividing the grades (grades I, II, III, and IV) according to the infiltration damage to a large number of infiltrated patients. The redistribution of fluid from the extracellular to intracellular space and/or the removal from the local region as may during the wound healing process after IV infiltration can be investigated using the impedance parameters such as the relative changes in resistance in zero frequency (R_0), resistance in infinity frequency (R_∞), and resistance in intracellular fluid (R_{ICF}) [29]. In addition, it would be also desirable to measure other impedance parameters such as phase angle (θ), characteristic frequency (f_C), bioelectrical impedance vector analysis (BIVA), for the detection of infiltration in various medical settings that occurs when blood is leaked from the vein or IV solution containing blood components or antibiotics is infused.

ACKNOWLEDGMENTS

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 (No. 2015R1A2A2A04003415).

REFERENCES

[1] N. E. Soifer, S. Borzak, and B. R. Edlin, "Prevention of peripheral venous catheter complications with an intravenous therapy team: a randomized controlled trial," *Archives of Internal Medicine*, vol. 158, no. 5, pp. 473-477, 1998.

[2] C. M. Rickard, J. Webster, M. C. Wallis, N. Marsh, M. R. McGrail, V. French et al., "Routine versus clinically indicated replacement of peripheral intravenous catheters: a randomized controlled equivalence trial," *Lancet*, vol. 380, no. 9847, pp. 1066-1074, 2012.

[3] J. Webster, S. Osborne, C. Rickard, and J. Hall, "Clinically-indicated replacement versus routine replacement of peripheral venous catheters," *Cochrane Database of Systematic Reviews*, vol. 17, no. 3, article ID. CD007798, 2010.

[4] Infusion Nurse Society, "Infusion nursing standards of practice," *Journal of Infusion Nursing*, vol. 29, S1-S92, 2006.

[5] R. Clifton-Koeppel, "Wound care after peripheral intravenous extravasation: what is evidence?" *Newborn and Infant Nursing Reviews*, vol. 6, pp. 202-211, 2006.

[6] L. Hadaway "Infiltration and extravasation," *American Journal of Nursing*, vol. 107, no. 8, pp. 61-72, 2007.

[7] J. L. Thigpen, "Peripheral intravenous extravasation: Nursing procedure for initial treatment," *Neonatal Network*, vol. 26, no. 6, pp. 379-384, 2007.

[8] M. M. Pollack, "Intravenous infiltration detection," U.S. Patent 20130131506 A1, Nov. 18, 2011.

[9] S. Doinger, P. Ishimine, J. C. Fox, and J. T. Kanegaye, "Randomized controlled trial of ultrasound-guided peripheral intravenous catheter placement versus traditional techniques in difficult-access pediatric patients," *Pediatric Emergency Care*, vol. 25, no. 3, pp. 154-159, 2009.

[10] F. Magnarelli, "IV Infiltration Detector," 2013 [Internet]. Available: http://contest.techbriefs.com/2013/entries/medical/3251.

[11] L. W. Winchester and N. Y. Chou, "Optical detection of intravenous infiltration," in *Advanced Biomedical and Clinical Diagnostic Systems IV, Proceedings of the SPIE vol. 6080*. Bellingham, WA: SPIE, 2006.

[12] N. Y. Chou, L .W. Winchester, W. J. Naramore, M. S. Alley, and A. J. Lesnick, "An optical device for detecting intravenous infiltration," 2006 [Internet]. Available: http://www.ivteam.com/optical-iv.pdf.

[13] H. C. Lukaski, P. E. Johnson, W. W. Bolonchuk, and G. I. Lykken, "Assessment of fat-free mass using bioelectrical impedance measurement of the human body," *American Journal of Clinical Nutrition*, vol. 41, no. 4, pp. 810-817, 1985.

[14] M. S. Mialich, J. M. F. Sicchieri, and A. A. J. Junior, "Analysis of body composition: a critical review of the use of bioelectrical impedance analysis," *International Journal of Clinical Nutrition*, vol. 2, no. 1, pp. 1-10, 2014.

[15] S. F. Khalil, M. S. Mohktar, and F. Ibrahim, "The theory and fundamentals of bioimpedance analysis in clinical status monitoring and diagnosis of diseases," *Sensors*, vol. 14, no. 6, pp. 10895–10928, 2014.

[16] L. C. Ward, "Segmental bioelectrical impedance analysis: an update," *American Journal of Clinical Nutrition*, vol. 15, no. 5, pp. 424-429, 2012.

[17] H. C. Lukaski, "Biological indexes considered in the derivation of the bioelectrical impedance analysis," *American Journal of Clinical Nutrition*, vol. 64, no. 3, pp. 397S-404S, 1996.

[18] C. Pichonnaz, J. P. Bassin, E. Lecureux, D. Currat, and B. M. Jolles, "Bioimpedance spectroscopy for swelling evaluation following total knee arthroplasty: a validation study," *BMC Musculoskeletal Disorders*, vol. 16, article no. 100, 2015.

[19] D. B. Stroud, B. H. Cornish, B. J. Thomas, and L. C. Ward, "The use of Cole-Cole plots to compare two multi-frequency bioimpedance instruments," *Clinical Nutrition*, vol. 14, no. 5, pp. 307-311, 1995.

[20] S. Grimnes and O. G. Martinsen, *Bioimpedance and Bioelectricity Basics*, 2nd ed. Oxford: Elsevier, 2008.

[21] F. Zhu, E. F. Leonard, and N. W. Levin, "Body composition modeling in the calf using an equivalent circuit model of multi-frequency bioimpedance analysis," *Physiological Measurement*, vol. 26, no. 2, pp. S133-S143, 2005.

[22] J. H. Kim, S. S. Kim, S. H. Kim, S. W. Baik, and G. R. Jeon, "Bioelectrical impedance analysis at popliteal regions of human body using BIMS," *Journal of Sensor Science & Technology*, vol. 25, no. 1, pp. 1-7, 2016.

[23] B. C. Kim, C. M. Kim, and C. H. Lee, "Multi-channel impedance measuring method and multi-channel impedance measuring instrument," WO 2014035040 A1 (PCT/KR2013/005779), Jun. 28, 2013.

[24] U. Mulasi, A. J. Kuchnia, A. J. Cole, and C. P. Earthman, "Bioimpedance at the bedside: current applications, limitations, and opportunities," *Nutrition in Clinical Practice*, vol. 30, no. 2, pp. 180-193, 2015.

[25] I. Haapala, A. Hirvonen, L. Niskanen, M. Uusitupa, H. Kroger, E.

Alhava, and A. Nissinen, "Anthropometry, bioelectrical impedance and dual-energy X-ray absorptiometry in the assessment of body composition in elderly Finnish women," *Clinical Physiology and Functional Imaging*, vol. 22, no. 6, pp. 383-391, 2002.

[26] S. M. Weinstein, *Plumer's Principles & Practice of Intravenous Therapy*, 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2001.

[27] S. M. Park, I. S. Jeong, K. L. Kim, K. J. Park, M. J. Jung, and S. S. Jun, "The effect of intravenous infiltration management program for hospitalized children," *Journal of Pediatric Nursing*, vol. 31, no. 2, pp. 172-178, 2016.

[28] B. F. Tofani, S. A. Rineair, C. H. Gosdin, P. M. Patricia, S. McGee, K. R. Varadarajan, and P. J. Schoettker, "Quality improvement project to reduce infiltration and extravasation events in a pediatric hospital," *Journal of Pediatric Nursing*, vol. 27, no. 6, pp. 682-689. 2012.

[29] L. C. Ward, K. Sharpe, D. Edgar, V. Finlay, and F Wood, "Measurement of localized tissue water – clinical application of bioimpedance spectroscopy in wound management," *Journal of Physics: Conference Series*, vol. 434, pp. 012043, 2013.

Jaehyung Kim
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 a visiting scientist at Liquid Crystal Institute of Kent State University, USA in 1993, and also visiting professor at Physics Department of Portland State University, USA, in 2003. He is currently an honorary professor of computer simulation at Inje University and researcher at research institute of Nursing Science, Pusan Natioanl University, and has deep interest in bioelectrical impedance, electrodernal activity, and electrical stimulator, etc.

Beumjoo Shin
is a professor of applied IT and engineering, Pusan National University. His major is embedded system, MT connect and ROS. He is currently working on early infiltration detection system, and MT connect system applied with ROS.

Gyerok Jeon
received B.S. and M.S. degree from Pusan National University, Korea, 1978 and 1982, respectively. And doctor degree from Dong-A University Korea, 1993. He is currently professor, Department of Biomedical Engineering, Pusan National University School of Medicine, and working at Pusan National University Yangsan Hospital. His major is biomedical signal processing and biomedical measurement system.