Design of an Automatic System for Bioelectrical Impedance Phase Angle Measurement Using an Analog Multiplier

Vu Duy Hai, Vu Hoang Chuong, Hoang Trong Nam, Nguyen Ngoc Tram, Chu Quang Dan, and Dinh Thi Nhung

Abstract Phase angle (PA), related to bioelectrical impedance, detects changes in tissue electrical properties. Because of being dependent on body cell mass and cell membrane functions, PA has been considered a prognostic indicator in several clinical diseases such as HIV, chronic pulmonary disease, colorectal cancer, and breast cancer. PA has attracted considerable interest and has been frequently referred to as a global health marker within the clinical nutrition community research on cellular health. Therefore, this study is aimed to design a system for automatically measuring the phase angle with high accuracy of an individual body segment after excitation by a current source. The phase angle measuring system comprised a sine-wave generator, a low-intensity, high-frequency (100 kHz) current pump, a phase difference-to-voltage converter, and a high-resolution analog-to-digital converter (ADC). The design of the phase difference-to-voltage converter was based on a high-precision analog multiplier and a peak detector. The phase difference-to-voltage converter's performance assessment was conducted by applying two programmable phase-difference signals generated by the pulse generator to ensure the accuracy of the phase angle difference. The converted phase angle was then read by a 16-bit ADC and displayed. The two identical-frequency sine-wave signals were programmatically generated with phase angle difference step of 10° ranged from 10° to 90° for phase difference to voltage converter inputs. The measurement showed the error of 0.5° ± 0.2° (mean ± standard deviation) for the overall nine phase angle difference steps.

Keywords Phase angle (PA) · Bioelectrical impedance analysis (BIA) · Analog multiplier · Peak detector

---

V. D. Hai (✉) · V. H. Chuong · H. T. Nam · N. N. Tram · C. Q. Dan · D. T. Nhung
Biomedical Electronics Center, Hanoi University of Science and Technology, Hanoi, Vietnam
e-mail: hai.vuduy@hust.edu.vn

V. Van Toi et al. (eds.), *8th International Conference on the Development of Biomedical Engineering in Vietnam*, IFMBE Proceedings 85,
https://doi.org/10.1007/978-3-030-75506-5_11

1 Introduction

Disease-related malnutrition is an extensive problem in most healthcare settings. In cancer patients, malnutrition is a common demonstration and a major contributor to morbidity and mortality [1]. Malnutrition is characterized by changes in cellular membrane integrity and alterations in fluid balance [2]. Hence, body composition analysis is an important part of the overall nutritional evaluation in cancer patients [3, 4]. Factually, nutrition status has been assessed by several methods, including using objective parameters such as anthropometric (weight change, height change, body mass index (BMI), body circumference and skinfold thickness), subjective global assessment (SGA), and laboratory measures (measuring serum proteins such as albumin, transferrin, retinol-binding protein) [5]. However, most of them have shown limitations in terms of application. Anthropometric measures are impracticable in clinical settings because they are time-consuming and require well-trained staff. Some of the objective measurements, such as albumin serum one, are probably affected by many non-nutritional factors [5–8].

Additionally, the assessment of nutritional status changes in a short period becomes difficult because some objective parameters, such as albumin, have long half-lives. Bioelectrical Impedance Analysis (BIA), a little-used tool to evaluate nutritional status, can overcome some of these challenges. This technique is a portable method developed in recent decades that combines morphological and functional evaluation [9]. BIA is a safe, non-invasive, and consistent method for evaluating body composition in clinical practice.

BIA has been considered a method to estimate the body composition and evaluate the nutritional status of many patients with various diseases, including cancer patients [1, 10]. Nevertheless, instead of measuring body composition directly, BIA measures two bioelectrical indicators: resistance (R) and reactance (X_C) [11]. When an alternating current with low amplitude and high frequency flows through tissues, R is the opposition of total body water to the flow of that current [12, 13], related to extracellular and intracellular fluid [14]. X_C is the opposition proffered by the current flowing through capacitance produced by tissue interface and cell membranes [14, 15]. Namely, it reflects cell membranes' ability to function as capacitors providing reactance when the alternating current flows through tissues [13]. X_C is related to the cell membrane structure and function [16], i.e., it is related to extracellular and intracellular fluid balance, which are independent of cell membrane integrity [17]. The relationship between capacitance and resistance reflects different electrical properties of tissues affected in different ways by disease, nutritional status, and hydration status [18]. There is a low-amplitude high-frequency electric current (500–800 μA at 100 kHz) flowing through some electrodes placed on the hand and foot to evaluate body composition. Capacitance is the inducement that causes the current phase to lag behind the voltage phase, thus creates a phase shift between them. Geometrically, this shift is calculated based on the angular transformation of the capacitance to resistance ratio called the Bioelectrical Impedance Phase Angle (BIPA) [11]. BIPA is the angle created by the impedance vector and the resistance vector; it is calculated using

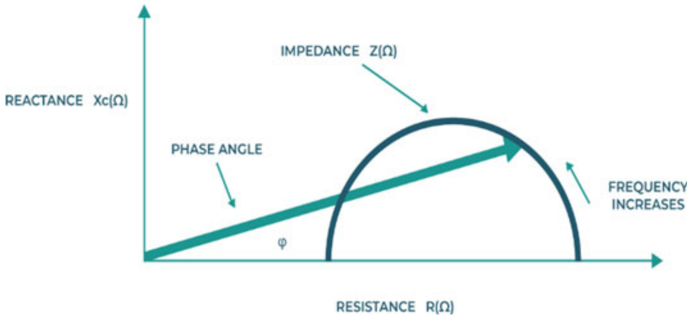

Fig. 1 BIA vector and phase angle

the arctangent of the ratio X_C in degrees [9]. The geometrical relationships among R impedance, reactance (X_C), resistance (R), phase angle, and frequency of the current are illustrated in Fig. 1.

When an electric current is applied to the human body, a portion of the current is stored in cell membranes, creating a BIPA, which is also the phase shift between the impedance and resistance vectors [11]. Consequently, the measured BIPA is governed by many objective factors such as the number of cells with their respective cell membranes, cell membrane integrity, related permeability, the amounts of extra and intracellular fluids [19], and body cell mass (BCM). BIPA might be changed if any changes occur in BCM, either functional defects of cell membranes [2]. By assessing BIPA, it can be concluded that it reflects the relative contributions of fluids (resistance) and cellular membranes (capacitance) of the human body. Low phase angle values suggest cell death or decreased cell integrity, while higher values suggest large quantities of intact cell membranes [9]. BIPA has been considered a prognostic indicator in various clinical situations like HIV, chronic pulmonary disease, colorectal cancer because it may indicate functional changes in the cell membrane and fluid balance [15, 18, 20, 21]. The present study's primary purpose is to design a system for automatically measuring the bioelectrical impedance phase angle with high accuracy of an individual body segment after excitation by a current source.

2 Methods and Materials

The phase angle measuring system is comprised of a sine-wave generator, a low intensity, high-frequency (100 kHz) current pump, a phase difference-to-voltage converter, and a high-resolution analog-to-digital converter (ADC). The design of the phase difference-to-voltage converter is based on a high-precision analog multiplier and a peak detector. The phase difference-to-voltage converter's performance assessment was conducted by applying two programmable phase-difference signals

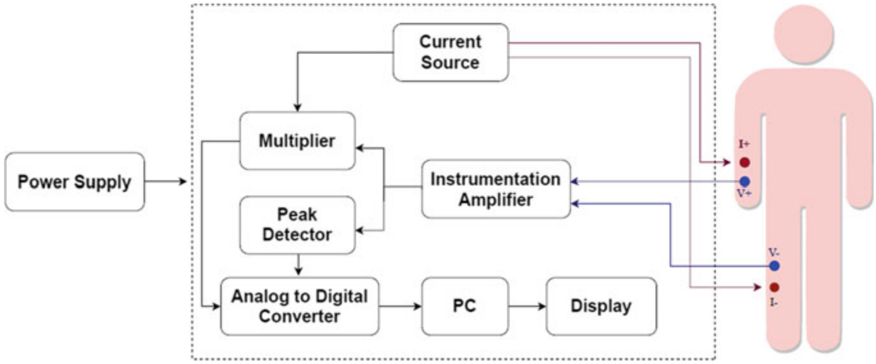

Fig. 2 Block diagram of hardware design

generated by the pulse generator to ensure the accuracy of the phase angle difference. The converted phase angle was then read by a 16-bit ADC and displayed. The proposed research aims to develop a system for measuring electrical impedance phase angle of body segments with help from a combination of some low cost, compact, reliable, and easy design circuits. The system block diagram and circuit design are illustrated in Fig. 2 [22–24].

2.1 Electrode Method

Four-electrode BIA is an informative, accurate, easy to perform, and affordable method of determining joints' impedance. The skin contact electrodes are constituted of Ag/AgCl material used mostly in bio-impedance applications [25].

2.2 Power Supply

The power unit is responsible for supplying power to the entire system. In which the current source block uses chips with a source of ±12V DC and ±15V DC. The analog signal receiving unit uses a source of ±15V DC. The digital processing unit and LCD use 5VDC power. The measurement circuit is powered by the DC-DC converter (JHM1524D12, XP Power, China) with voltage isolation of 4 kV, specifically designed for medical application, to ensure the electrical safety for measuring objects.

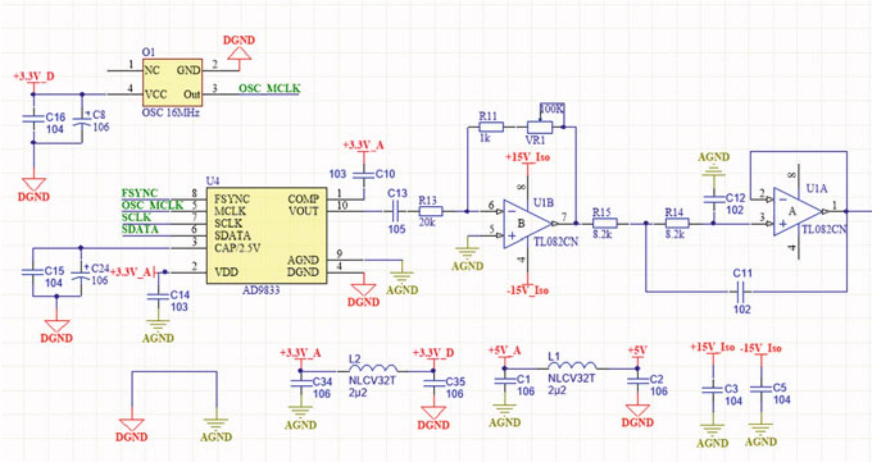

Fig. 3 Schematic of the current source unit

2.3 Current Source

In this design, the improved Howland Current Pump Topology (Fig. 3) is selected for the voltage-current converter due to its ability to provide bi-polar output current, wide frequency range, high output impedance and temperature stability. However, this topology has one drawback: it requires very precise resistors to match the ratio and an op-amp with high open loop gain and high CMRR to achieve a high output impedance current source, especially with high-frequency waveform. Because in bioimpedance measurements, the current source directly affects the quality of the recorded signal. The authors take careful consideration of PCB layout, selection of precise resistors (0.1% tolerance), and the op-amp to ensure the current source's quality. OPA2211 is used due to prominent features such as its low noise density, low voltage, low current noise and high speed.

In this study, a sine-wave high-frequency current source with an amplitude of 4 mA and a frequency of 100 kHz is injected into the body through two electrodes; the induced voltage is picked up by using another pair of electrodes. To ensure patient safety, any residual DC offset component is blocked by a high-pass filter [26–28].

2.4 Instrumentation Amplifier

The body segment's differential signals are fed to the instrumentation amplifier (INA129, Texas Instruments), which amplifies the signals from the body. A band-pass filter suppresses any unwanted noises outside of the signal band. This design's filter type is the 2nd-order Butterworth active filter, which ensures the maximal

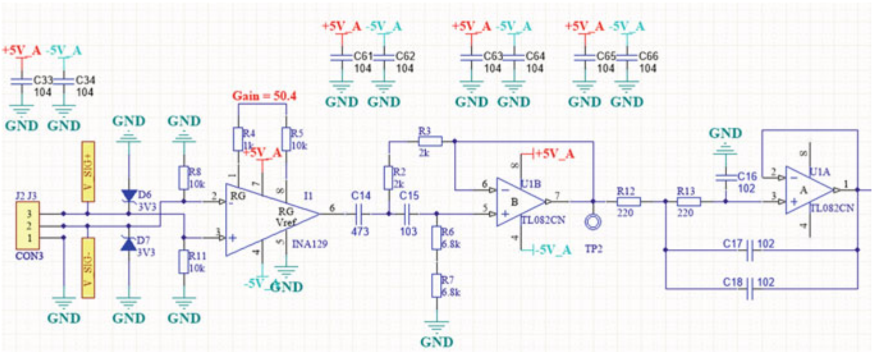

Fig. 4 Schematic of the amplifier unit

flatness and phase linearity, according to Sallen-Key topology, with a passband of 80–120 kHz. The schematic of the amplifier unit is shown in Fig. 4.

2.5 Bioelectrical Impedance Phase Angle Measurement Unit

The current is injected simultaneously into the body segment and a well-known reference resistor (470 Ω) in series. The voltage across the reference resistor and the instrumentation amplifier's signal is then fed to the multiplier IC (Analog Devices). The output voltage of AD633 is calculated as the following formula.

$$V = \frac{A.B}{2 \times SF} \cos \varphi \tag{1}$$

A is the amplitude of the reference signal, B is the amplitude of the signal attained from the body, SF is an adjusted scale factor of IC AD633, φ is the phase difference between the reference signal and the signal attained from the body. B is determined by a high-precision, high-speed peak detector unit. The schematic of the peak detector unit is illustrated in Fig. 5.

The phase difference-to-voltage converter includes an analog multiplier using a high-precision voltage reference generator and an active low-pass filter. The detailed schematic of the phase difference-to-voltage converter is illustrated in Fig. 6.

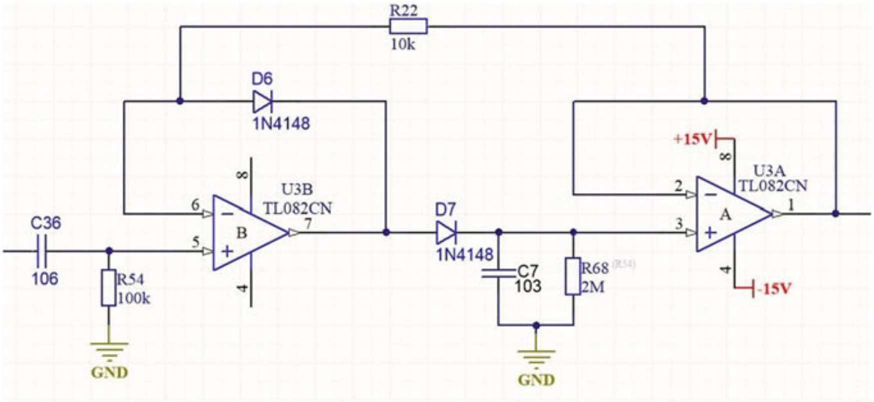

Fig. 5 Schematic of the peak detector unit

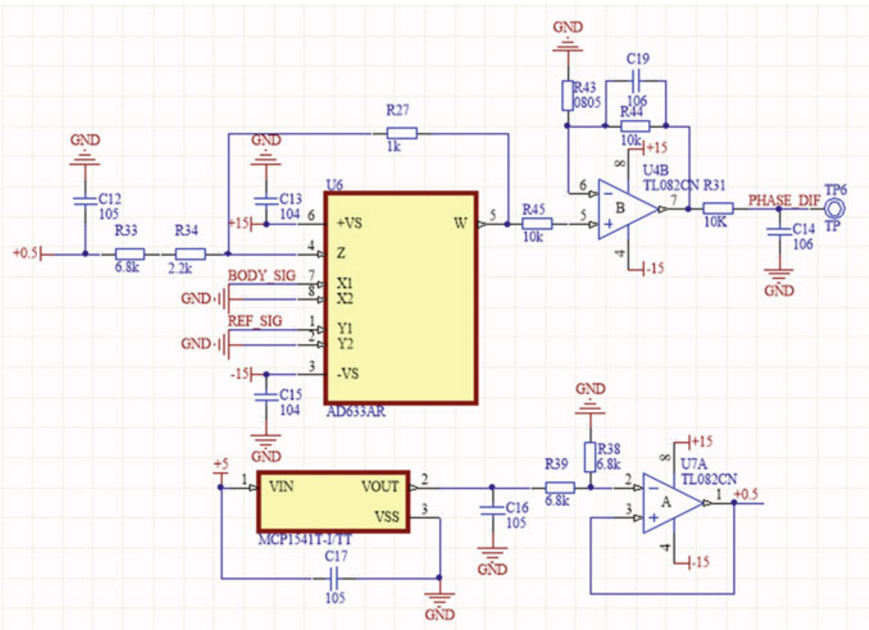

Fig. 6 Schematic of the multiplier unit

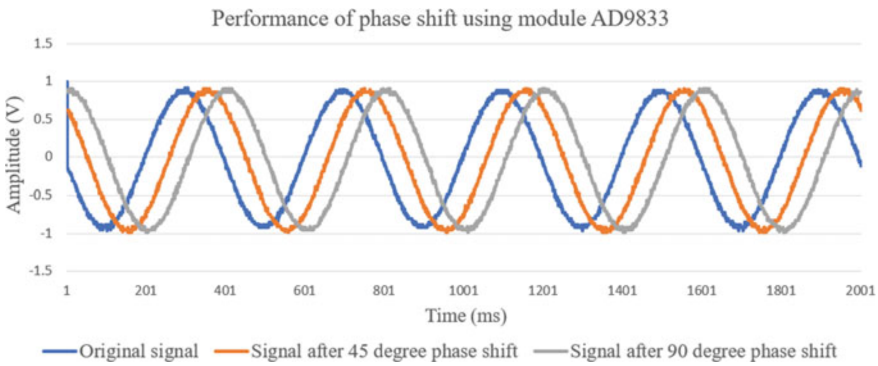

Fig. 7 The two generated sine-wave signals at a phase difference of 90° and 45°

3 Results and Discussion

3.1 Assessment of the Sine-Wave Generator Using AD9833

The designed generator using AD9833 can simultaneously generate two sine-wave signals with the precise programmable frequency range of 50–200 kHz and phase difference range of 0° to 180°. Figure 7 shows examples of the two generated sinewave signals at phase differences of 90° and 45°, respectively. The data used in the figures was sampled and extracted from a digital oscilloscope (MSOX2024A, KEYSIGHT).

Figure 7 demonstrates that setting up two signals with a custom phase difference using AD9833 gives the desired result. The accuracy of the two signals helps reduce the error of the results obtained from the phase shift measurement unit; thus, they are more accurate.

3.2 Assessment of the Current Source

The ability to supply a constant current independent of load resistance is the most important technical specification of the current source. To assess the current source, the current amplitude was fixed at the value of 1 mA; then the load resistors were changed within resistor values of 100 Ω, 220 Ω, 560 Ω, 680 Ω, 1 kΩ, 1.2 kΩ, 2 kΩ, 5.1 kΩ, and 10 kΩ. The voltage dropping in the load resistors was then measured to plot a dependency graph (Fig. 8) of the load resistance and the voltage to check the linearity in a certain range of resistors that the current source is designed to meet. From the figure, we can conclude that the curve is linear, with the load's resistance smaller than 4 kΩ. This means the maximum load which the current source can supply without distortion. It is approximately 4 kΩ.

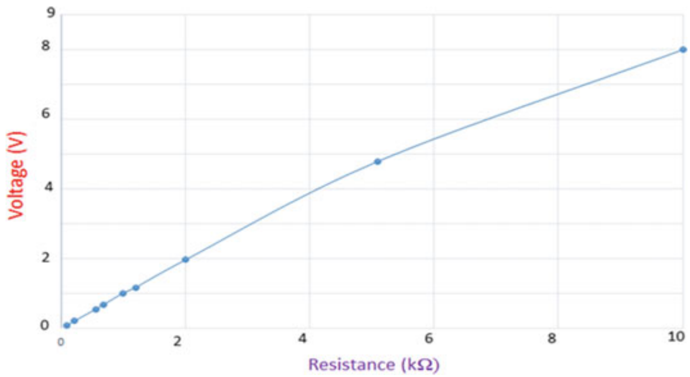

Fig. 8 Voltage–load dependency graph

While the body's internal impedance is less than 1181 Ω [29], the resistance of the load used in this assessment ranges from 0 to 4 kΩ in which the supplied constant current is independent of the load resistance. This means the current source will work effectively when the proposed system is used for body measurements without harming the patients.

3.3 Assessment of the Phase Angle Measuring Unit

This sub-section evaluates the accuracy of the phase angle measurement circuit. The evaluation is based on comparing the phase difference between the setup values and the measuring results. The two identical-frequency sine-wave signals were programmatically generated with phase angle difference step of 10° and ranged from 10° to 90° for phase difference-to-voltage converter inputs. A 12-bit ADC then sampled the signal with the sampling rate of 100 samples/s. The measuring phase angle values are shown in Table 1. The measuring results show the error of 0.5° ± 0.2° (mean ± standard deviation).

Figure 9 illustrates the correlation between measuring phase values and setup phase values. The proposed system's measuring results have a high correlation with the setup values (coefficient of determination $R^2 = 0.997$).

The results obtained from the measuring circuit give an acceptable error of 0.5° ± 0.2°over the range of 10° to 90°. Adjusting methods and the deviation of component values are the main factors causing the error above. These results show that the proposed system built on the given method is feasible and performs the desired function. When performing bioelectric impedance phase angle measurements, the results obtained in colorectal cancer patients range from 2° to 8° [18]; the thresholds used for classification at advanced cancer patients or liver cirrhosis ones are also below 10° [1, 9]. Hence the authors want to continue to improve the system, narrow the measuring range to 0 to 10° and increase the accuracy of the measurement results.

Table 1 The table of setup and measuring phase angle results

Measurement No.	Setup phase angle value	Measuring phase angle value 1
1	10	10.26
2	20	20.75
3	30	30.8
4	40	40.6
5	50	50.49
6	60	60.29
7	70	70.11
8	80	79.85
9	90	89.5

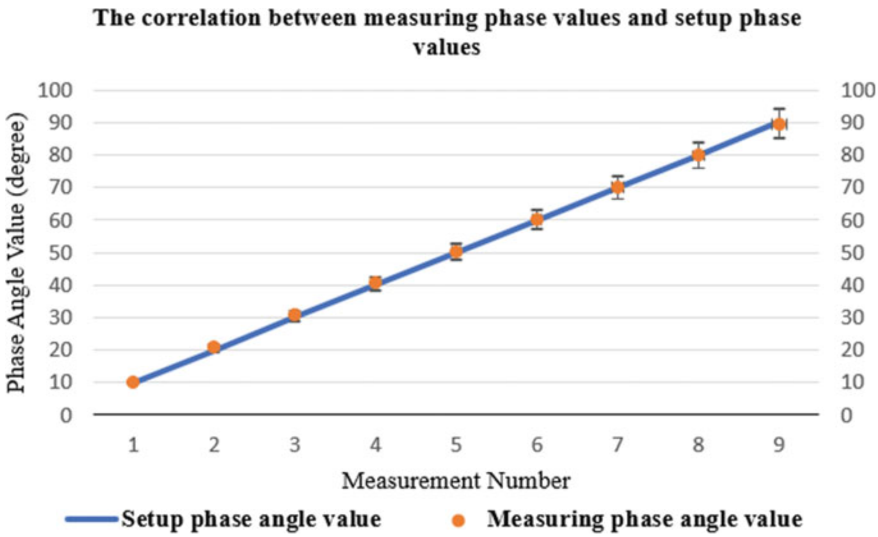

Fig. 9 The correlation between measuring phase values and setup phase values

Then, the direct measurement of the BIPA index on the body applied to monitor patients' nutritional status will bring great value.

4 Conclusion

Based on the results and analysis described earlier, the proposed measuring system works effectively in the measuring range and performs the desired function. This system offers an ability to automatically measure the bioelectrical impedance phase angle with low error. The initial results of this study are promising. They can be potentially developed to become instrumentation devices capable of detecting the bioelectrical impedance phase angle to support the clinical diagnosis and research purposes. The overall evaluation of the system could be temporarily performed on a well-known R-C model. In further studies, the authors would assess the system on individual body segments after meeting the safeguards and being approved by the ethics committee for clinical and research applications. The results would be published in further studies.

Acknowledgements The authors would like to acknowledge the support of the Biomedical Electronics Center (BMEC), School of Electronics and Telecommunications (SET), the university clinic, Hanoi University of Science and Technology (HUST).

Conflict of Interest No potential conflict of interest was reported by the authors.

References

1. Sarhill N, Mahmoud FA, Christie R, Tahir A (2003) Assessment of nutritional status and fluid deficits in advanced cancer. Am J Hosp Palliat Care 20:465–473
2. Barbosa-Silva MC, Barros AJ, Post CL, Waitzberg DL, Heymsfield SB (2003) Can bioelectrical impedance analysis identify malnutrition in preoperative nutrition assessment? Nutrition 19:422–426
3. Cox-Reijven PL, van Kreel B, Soeters PB (2003) Bioelectrical impedance measurements in patients with gastrointestinal disease: validation of the spectrum approach and a comparison of different methods for screening for nutritional depletion. Am J Clin Nutr 78:1111–1119
4. Fredrix EW, Saris WH, Soeters PB et al (1990) Estimation of body composition by bioelectrical impedance in cancer patients. Eur J Clin Nutr 44:749–752
5. Bauer J, Capra S, Ferguson M (2002) Use of the scored Patient Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. Eur J Clin Nutr 56:779–785
6. Carney DE, Meguid MM (2002) Current concepts in nutritional assessment. Arch Surg 137:42–45
7. Waitzberg DL, Correia MI (2003) Nutritional assessment in the hospitalized patient. Curr Opin Clin Nutr Metab Care 6:531–538
8. Detsky AS, Baker JP, Mendelson RA, Wolman SL, Wesson DE, Jeejee-bhoy KN (1984) Evaluating the accuracy of nutritional assessment techniques applied to hospitalized patients: methodology and comparisons. JPEN J Parenter Enteral Nutr 8:153–159
9. Selberg O, Selberg D (2002) Norms and correlates of bioimpedance phase angle in healthy human subjects, hospitalized patients, and patients with liver cirrhosis. Eur J Appl Physiol 86(6):509–516
10. Simons JP, Schols AM, Westerterp KR, ten Velde GP, Wouters EF (1995) The use of bioelectrical impedance analysis to predict total body water in patients with cancer cachexia. Am J Clin Nutr 61:741–745
11. Baumgartner RN, Chumlea WC, Roche AF (1988) Bioelectric impedance phase angle and body composition. Am J Clin Nutr 48:16–23
12. Toso SPA, Gusella M, Menon D, Bononi A, Crepaldi G et al (2000) Altered tissue electric properties in lung cancer patients as detected by bioelectric impedance vector analysis. Nutrition 16(2):120–124
13. Mattar JÁ (1996) Application of total body bioimpedance to the critically ill patient. Brazilian Group for bioimpedance study. New Horiz 4(4):493–503

14. Piccoli A, Nescolarde LD, Rosell J (2002) Análisis convencional y vectorial de bioimpedância en la práctica clínica. Nefrologia 22(3):228–238
15. Scwenk A, Beisenherz A, Romer K, Kremer G, Salzberger B, Elia M (2002) Phase angle from bioelectrical impedance analysis remains an independent predictive marker in HIV infected patients in the era of highly active antiretroviral treatment. Am J Clin Nutr 72(2):496–501
16. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gómez JM et al (2004) Bioelectrical impedance analysis-part I: review of principles and methods. Clin Nutr 23(5):1226–1243
17. De Lorenzo A, Barra FPA, Sasso GF, Battistini NC, Deureberg P (1991) Body impedance measurements during dialysis. Eur J Clin Nutr 45:321–325
18. Gupta D, Lammersfeld CA, Burrows JL, Dahlk SL, Vashi PG, Grutsch JF et al (2004) Bioelectrical impedance phase angle in clinical practice: implications for prognosis in advanced colorectal cancer. Am J Clin Nutr 80(6):1634–1638
19. Barbosa-Silva MC, Barros AJ (2005) Bioelectrical impedance analysis in clinical practice: a new perspective on its use beyond body composition equations. Curr Opin Clin Nutr Metab Care 8:311–317
20. Faisy C, Rabbat A, Kouchakji B, Laaban JP (2000) Bioelectrical impedance analysis in estimating nutritional status and outcome of patients with chronic obstructive pulmonary disease and acute respiratory failure. Intensive Care Med 26:518–525
21. Mushnick R, Fein PA, Mittman N, Goel N, Chattopadhyay J, Avram MM (2003) Relationship of bioelectrical impedance parameters to nutrition and survival in peritoneal dialysis patients. Kidney Int Suppl 87:S53–S56
22. Ngoc PP, Hai VD, Bach NC et al (2015) EEG signal analysis and artifact removal by wavelet transform. In: The 5th international conference on biomedical engineering in Vietnam. IFMBE proceedings, vol 46. Springer, Cham
23. Hai VD, Thuan ND (2010) Design of laboratory information system for healthcare in Vietnam BK-LIS. In: The 3rd international conference on communications and electronics, art. no. 5670692, pp 110–114
24. Vu HD, Nguyen TD, Pham NP et al (2010) A design of renal dataflow control and patient record management system for renal department environment in Vietnam. In: The third international conference on the development of biomedical engineering in Vietnam. IFMBE proceedings, vol 27. Springer, Berlin
25. Hai VD, Hung PD, Hung PM et al (2019) Design of noninvasive hemodynamic monitoring equipment using impedance cardiography. In: The 7th international conference on the development of biomedical engineering in Vietnam. IFMBE proceedings, vol 69. Springer, Singapore
26. Hai VD, Hung PM, Trung LHP et al (2017) Design of software for wireless central patient monitoring system. In: Proceedings of KICS-IEEE international conference on information and communication with Samsung LTE&5G special workshop, Hanoi, Vietnam, pp 214–217
27. Hai VD (2021) Technique of receiving data from medical devices to create electronic medical records database. In: Soft computing applications and techniques in healthcare. CRC Press, Boca Raton. http://doi.org/10.1201/9781003003496
28. Hai VD, Hung PD, Dan CQ (2020) Modified electrode placements for measurement of hemodynamic parameters using impedance cardiography. J Med Eng Technol. http://doi.org/10.1080/03091902.2020.1799089
29. Agaa K, Taraoa H, Urushiharaa S (2016) Calculation of human body resistance at power frequency using anatomic numerical human model. Energy Procedia 89:401–407