Low Cost Dual Frequency Impedance Analysis for Measuring Internal and External Celluler Fluid

Khusnul Ain[1], R. Arif Wibowo[2], Soegianto Soelistiono[1], Lailatul Muniroh[3], Tri Agggono[2], and M.Rizky Yusdy[1]

[1]*Biomedical Engineering, Universitas Airlangga, Surabaya, Indonesia*
[2]*Physics, Universitas Airlangga, Surabaya, Indonesia*
[3]*Public Health, Airlangga University, Surabaya, Indonesia*

Keywords: Bioimpedance, dual frequency, extracellular, intracellular, low cost

Abstract: The regulation of body fluid balance is a major concern in body health. Disruption of body fluid balance is a major factor responsible for changes in cell volume. It can affect cell function and survival. Intracellular fluid (ICF), extracellular fluid (ECF) and total body fluid (TBW) have been used as information on body fat levels, dengue indications and some chronic diseases. The design and development of dual frequency bioelectrical impedance analysis prototype are used as a candidate for intracellular and extracellular fluid measuring instrument. The device was built using sine wave generator from ICL8038 which can produce 20 kHz and 75 kHz voltage controlled current source (VCCS) and from LF412 which can generate 0.5 mA from Howland dual op-amp method, potential was measured by instrument amplifier from AD620 and AD536 was used as AC to DC converter. The device performance was tested on 10 volunteers. The performance indicator is the relationship of ICF and ECF calculations to H^2/Z. The analysis of intracellular fluid (ICF) was obtained from used the measurement of total body impedance at high frequency of 75 kHz. It has excellent linearity with $R^2 = 0{,}9636$. Meanwhile, analysis of extracellular fluid (ECF) was obtained from the measurement of total body impedance at low frequency of 20 kHz. It has a very good linearity with $R^2 = 0.9579$..

1 INTRODUCTION

Dengue fever is an acute disease caused by dengue virus infection carried by mosquitoes Aedes aegypti and Aedes albopictus. The virus causes disruption of the capillary blood vessels in the blood clotting system resulting in bleeding. The dengue virus transmitted through the bite of Aedes aegypti and Aedes albopictus was previously infected by dengue virus from other dengue fever patients with 4 related antigens, but different serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) including the genus Flavivirus, family Flaviviridae (WHO, 2009).

The classification and definition of dengue fever is divided into dengue fever and dengue hemorrhagic fever. Dengue fever begins with a sudden increase in temperature with headache, myalgia, macular rash, loss of appetite, nausea, vomiting, abdominal pain, changes in psychological state, and thrombocytopenia, then if initial clinical management or appropriate fluid therapy is not provided, dengue fever will become a dengue hemorrhagic fever that begins with a fever that subsides but increases micro vascular permeability, decreases plasma volume, and is aggravated by hypotension and shock, lastly if appropriate therapy is not available, circulatory failure will occur, then dengue hemorrhagic fever will become dengue shock syndrome which is a fatal classification and definition of dengue that begins with a rapid and weak pulse.

Therefore, delays in the management of fluid therapy may lead to death (Deen *et al.*, 2006). The number of cases of dengue fever every year and the absence of vaccines and antiviral drugs that can stop dengue virus infection, result in broad loss impact, especially on economic and health aspects (WHO, 2009). Dengue virus that enters the body will infect immune cells in the skin tissue then enter the lymphatic system, thus, triggering a strong inflammatory reaction. During the incubation period, the virus replicates locally then spreads into the

Ain, K., Wibowo, R., Soelistiono, S., Muniroh, L., Anggono, T. and Yusdy, M.
Low Cost Dual Frequency Impedance Analysis for Measuring Internal and External Celluler Fluid.
DOI: 10.5220/0007545905040510
In *Proceedings of the 2nd International Conference Postgraduate School (ICPS 2018)*, pages 504-510
ISBN: 978-989-758-348-3

bloodstream which is commonly referred to as viremia. In some patients, especially children, dengue virus infection can lead to severe clinical manifestations. The most severe clinical manifestations can cause blood vessels to become permeable resulting in leakage of plasma which ultimately requires intensive hospital care. The phase and clinical symptoms when experiencing dengue fever is the first phase of high fever which is characterized by high fever reaches 40^{o}C with symptoms caused by severe headache, back pain in the eyes, nausea, vomiting, swollen glands, rash, pain muscles and joints. This is a sign that a person is infected with dengue virus after being bitten by an infected mosquito and an incubation period of dengue virus for 4 - 10 days, in this phase usually occurs for 2 - 7 days.

Accurate diagnosis and monitoring of dengue fever condition is needed to identify the severity level in providing appropriate treatment. In order to handle and control cases of dengue, there are many methods that have been developed and used to diagnose and monitor the risk of dengue fever. One of them is to observe the onset and progression of plasma leakage of dengue fever patients by measuring the increase in total hematocit or hemoglobin (WHO, 2009). The advantage of this method is not only to diagnose dengue fever but also to distinguish dengue fever as well, then by monitoring the number of thrombocyte of dengue fever patients and liver function. Although this conventional method has been able to provide an accurate diagnosis, it takes a long time, is invasive, and can harm patients, since this conventional method requires frequent invasive blood sampling, which can lead to further injury to the subcutaneous tissues and potentially harmful to people with dengue fever (Ibrahim *et al.*, 2005 and Ibrahim *et al.*, 2007). In addition, this conventional method can only be done in inpatients at the hospital only, but not all patients with dengue fever can undergo hospitalization because the facility in the hospital itself is not able to handle all patients with dengue fever in a very large number (Ibrahim *et al.*, 2005).

The facts show that cases of dengue fever are often misdiagnosed with other diseases, such as flu or typhoid. This is because the symptoms of dengue virus infection in the early stages may not have a distinctive feature (Ginanjar, 2008). So far, the majority of society and health practitioners in Indonesia still do not understand the difference between fever caused by dengue virus infection and common fever caused by other infections. This is what causes the number of morbidity (mortality rate) and mortality (Mortality Rate), because the success of the handling of dengue fever case is largely determined by early detection of dengue virus manifestations in patients so that it can be done case management in the form of management therapy effective fluids. Early detection of dengue fever patients with non-invasive method, one of them can be done through body temperature analysis because at the time of dengue fever patient experiencing high fever phase until critical phase, they will have fever which has characteristic marked with horse saddle graph produced by body temperature.

Multi-frequency bioelectrical impedance analysis (MF - BIA) method can diagnose the manifestation of dengue virus in dengue fever patient. This method uses a constant electric current at low frequencies of 5 kHz to 1000 kHz through the body, and produces a potential difference value (V) to obtain an impedance value (Z), using four electrodes (Jaffrin *et. al.*, 2008). The results showed that there was a correlation between the frequency value of body fluid measurements, where the low frequency values represent extracellular fluid values (ECF) and high frequency values represent intracellular fluid values (ICF), so the total body water (TBW) was obtained based on the sum of the fluid value extracellular (ECF) and intracellular fluid value (ICF). Several studies have been conducted to determine the intracellular and extracellular fluids (Moissl *et al.* 2006).

2 METHODS

In this research, the design and development of intracellular cell and extracellular cell impedance measuring device. The design of the device is shown in Figure 1.

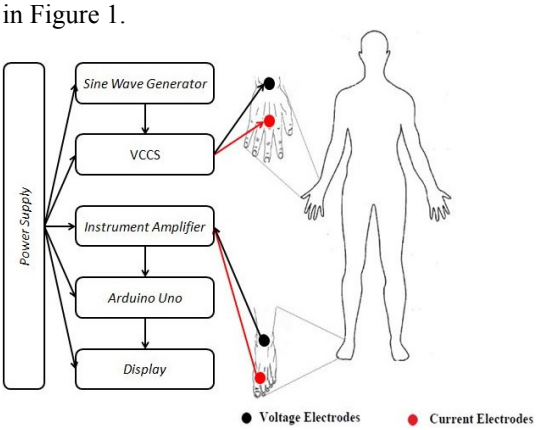

Figure 1 : Block diagram of *Bioelectrical Impedance Analysis*

The device consists of a sine wave generator, VCCS, voltage meter and microcontroller. Sine wave generator circuit was used as a generator of sinus voltage signal using IC IC8080 which was then connected with resistor and capacitor to produce sine voltage of 20 kHz and 75 kHz which can be seen in Figure 2.

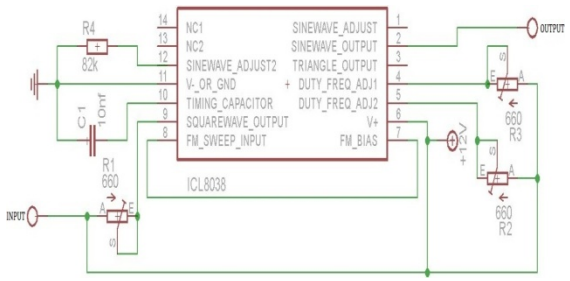

Figure 2 : Design of sine wave generator

Voltage Controlled Current Source (VCCS) circuit functions as electric current source based on input voltage signal. The VCCS circuit uses a dual opamp built from IC LF412 coupled with a resistor that can serve as a current source of 0.5 mA, as shown in Figure 3.

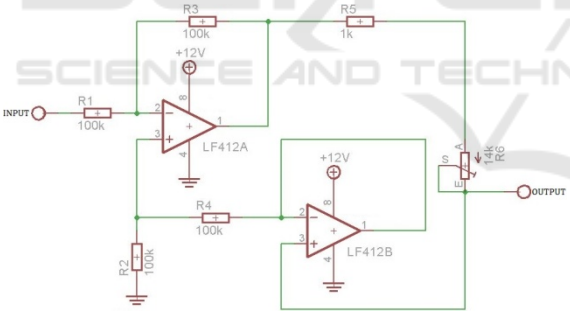

Figure 3 : Design of Voltage Control Current Source (VCCS).

The Instrument Amplifier circuit was used as a comparison of two input voltages into one output using IC AD620 which is then connected to the resistor as a reinforcement source, as in Figure 4.

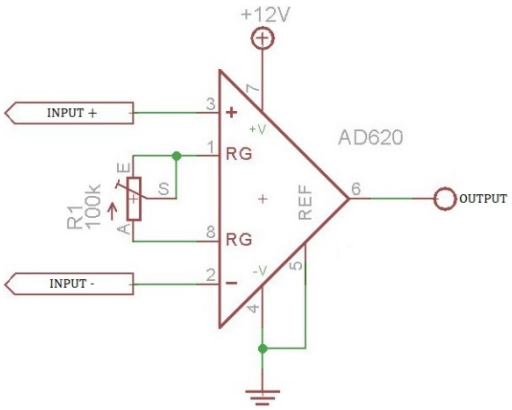

Figure 4 : Design of Instrument Amplifier

3 RESULT

Sinus generator built from IC IC8080 was coupled with capacitor 10 nF, resistor of 1650 Ω and 440 Ω respectively to produce sine voltage of 20 kHz and 75 kHz. The output signal generated by the circuit can be observed through the oscilloscope, as shown in Fig. 5 and Fig. 6.

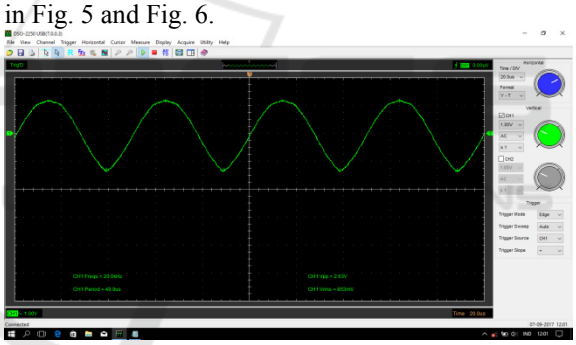

Figure 5 : Signal 20 kHz from sine wave generator

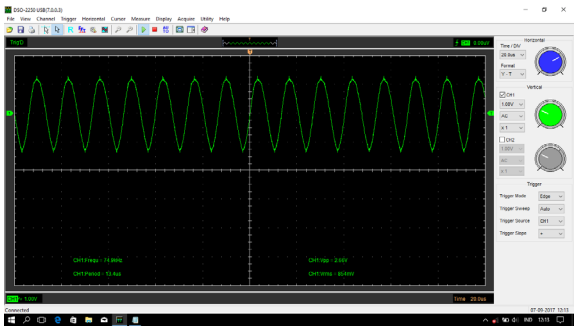

Figure 6 : Signal 75 kHz from sine wave generator

The output signal of the sine wave generator circuit produced a direct voltage (DC) that fluctuated from 4.80 V until 7.84 V. The VCCS circuit was used as an electric current generator based on input

voltage using LF412 IC. The circuit requires a supply voltage of ± 15V and a resistor to produce an electric current with a frequency of 20 kHz and 75 kHz with an electrical current ≤ 0.5 mA that is safe for the body. The output signal generated by the VCCS circuit can be observed through the oscilloscope shown in Figure 7.

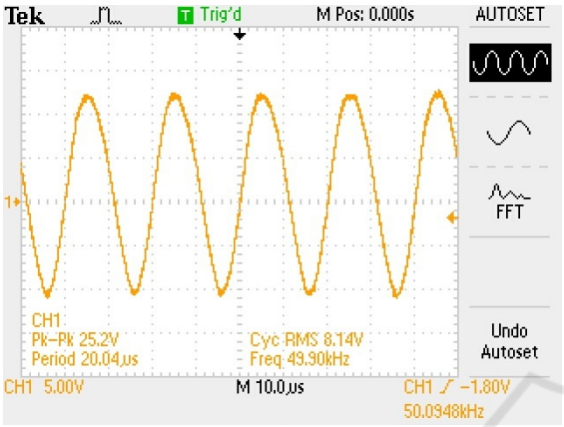

Figure 7 : The signal output from VCCS circuit

Based on the signal in the oscilloscope, it can be seen that the output signal from the VCCS circuit was a DC electric current that fluctuated from 3.52 V to 6.56 V. Furthermore, the VCCS circuit test showed the electric current generated against the load changes given in Figure 8.

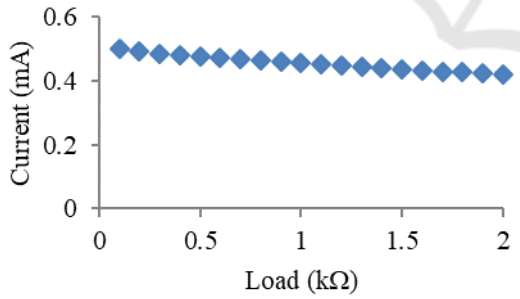

Figure 8. Graph between current and load at 50 kHz

The instrument amplifier circuit serves as a comparator of two inputs voltage into one output voltage. The circuit used an IC AD620 and ± 15V supply voltage connected to the resistor as the amplifier. The circuits used to tap the potential difference of the body from the electric current 20 kHz and 75 kHz. The circuits were channeled into the body using disposable electrodes that were bonded on the body surface. Based on the results shown in the oscilloscope, it appears that the output signal of the instrument amplifier circuit produced a DC voltage that fluctuated from 3.84 V to 7.36 V. The amplification of the instrument amplifier circuit is 1.5 as shown in Table 1.

Table 1 : Test of instrument amplifier

No.	Input (V)	Output (V)	Gain	Error (%)
1	1.24	1.82	1.47	2.15
2	2.06	3.10	1.50	0.32
3	3.22	4.78	1.48	1.04
4	4.18	6.16	1.47	1.75
5	5.10	7.57	1.48	1.05
6	6.11	9.14	1.50	0.27
7	7.03	10.45	1.49	0.90
8	8.25	12.41	1.50	0.28
9	9.09	13.49	1.48	1.06
10	10.16	15.03	1.48	1.38
Mean error				1.02

The signal generated by the instrument amplifier circuit can be observed through the oscilloscope, as displayed in Figure 9.

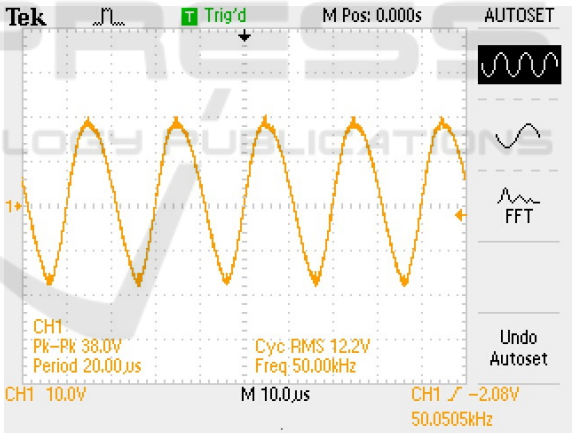

Figure 9 : Output signal from Instrument Amplifier

Dual frequency of bioelectrical impedance analysis tool as diagnostic candidate of dengue fever consists of hardware and software. The hardware was used as a generator of 20 kHz and 75 kHz sine wave signals with an electric current of ≤ 0.5 mA. Furthermore, the electric current was used to determine the impedance (Z) of the body.

The measurement of the potential difference (V) generated from the 20 kHz and 75 kHz sine wave signals was received by the instrument amplifier and processed by arduino uno microcontroller with the software. The software functions as a viewer and

data processor obtained from hardware. The software will read the potential of the body. The analog data were converted into bits. The bit was converted by arduino software IDE 1.6.9 into a volt / potential (V), the last result of the measurement of the potential (V) was processed by the software into an impedance using Equation (1).

$$Z = \frac{}{} \quad (1)$$

Equation 1 was obtained based on Figure 10.

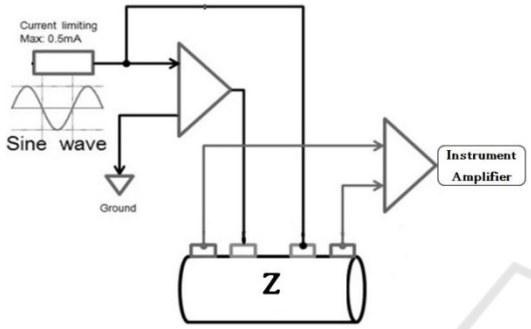

Figure 10 : Analogies of conventional calculations

The measurement of body impedance (Z) using Equation (1) was conducted by dividing the injected electric current (I) and the potential body (V) obtained from the instrument amplifier circuit. The problem that occurred when measuring the body impedance (Z) using equation (1) was when the electric current (I) was considered constant, because in fact in testing the voltage controlled current source (VCCS) circuit in which the electric current (I) is smaller when the load gets bigger. So when measuring the body impedance (Z) using equation (1) and assuming the value of electric current (I) constant at ≤ 0.5 mA, the resulting body impedance (Z) is not valid. Voltage divider approach is a valid method that can be used in measuring body impedance (Z), that is by using equation (2).

$$Z = \frac{}{}xR \quad (2)$$

Equation (2) was obtained from Figure 11.

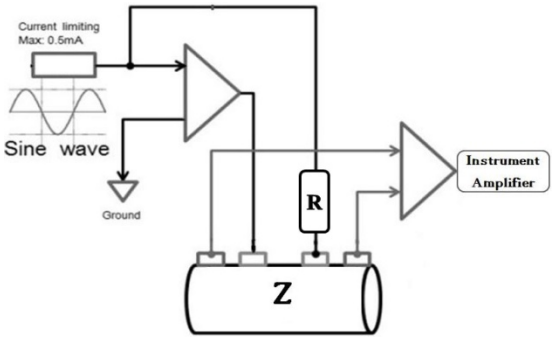

Figure 11 : Analogies of modification calculations

The measurement of body impedance (Z) using equation 2 was done by dividing the voltage (Vo) obtained from the reading of the potential at meeting point (R) and (Z) and the voltage of the current source Vs obtained from the reading the potential at point (R) then multiplied by the resistance (R) used. The results of device testing with variations of measurable barriers can be seen in Table 2 and 3.

Tabel 2 : Device testing with various loads at 20 kHz

No.	Impedance (Ω)	V_s (V)	V_o (V)	Measurement impedance (Ω)	Error (%)
1	1000	5.47	0.76	993.42	0.66
2	2000	5.09	1.44	2022.79	1.14
3	3000	4.51	1.92	3043.90	1.46
4	4000	4.13	2.30	3981.84	0.45
5	5000	3.65	2.58	5053.97	1.08
6	6000	3.62	3.07	6063.67	1.06
7	7000	3.48	3.45	7088.36	1.26
8	8000	3.06	3.43	8014.54	0.18
9	9000	3.04	3.81	8961.02	0.43
10	10000	2.80	3.89	9933.39	0.67
Mean error					0.84

Tabel 3 : Device testing with various load at 75 kHz

No.	Impedance (Ω)	V_s (V)	V_o (V)	Measurement impedance (Ω)	Error (%)
1	1000	4.89	0.67	997.46	0.25
2	2000	4.35	1.19	1991.54	0.42
3	3000	4.13	1.71	3014.24	0.47
4	4000	3.81	2.08	3974.38	0.64
5	5000	3.48	2.40	5020.69	0.41
6	6000	3.27	2.72	6055.54	0.93
7	7000	3.02	2.93	7063.05	0.90
8	8000	2.94	3.24	8022.86	0.29
9	9000	2.70	3.32	8951.70	0.54
10	10000	2.56	3.45	9810.94	1.89
Mean error					0.67

After the device was well-tested, it was used to measure impedances of 10 volunteers at frequencies of 20 kHz and 75 kHz. The data test were taken by measuring weight, height, and total body impedance. The data were then used to determine the intracellular fluid (ICF), extracellular fluid (ECF), and total body water (TBW), while the results of data retrieval device that has been done can be seen in Table 4.

The measuring body fluids is based on the equation obtained by Hoffer *et al.*, in his journal entitled Correlation of Whole - Body Impedance with Total Body Water Volume (1969). The equation relates between total body impedance and total body fluids calibrated by dissolution techniques tritium in-vivo. Furthermore, the equation was used on 10 Volunteers. This is the example of the x volunteer:

- Height (H) = 168 cm
- Weight (W) = 70 kg
- It is obtained impedance (Z) = 937 Ω when Frequency was 20 kHz and impedance (Z) = 682 Ω was obtained when Frequency was 75 kHz

The calculation of intracellular fluid (ICF), extracellular fluid (ECF), and total body water (TBW), along with percentage of intracellular fluid value (ICF) and extracellular fluid (ECF) to total body fluids (TBW) is,

- Intracelular Cell Fluid (ICF)
  Y = 0.5855(X) + 1.9878
  ICF = 0.5855 x (168^2/682) + 1.9878
  ICF = 26.22
- Extracelular Cell Fluid (ECF)
  Y = 0.5855(X) + 1.9878
  ECF = (0.5855 x (168^2/937) + 1.9878)
  ECF = 19.62
- Total Body Water (TBW)
  TBW = ICF + ECF
  TBW = 26.22 + 19.62
  TBW = 45.84
- Percentage of ICF and ECF
  - Percentage of ICF
    %ICF = (ICF/TBW) x 100%
    %ICF = (26.22/45.84) x 100%
    %ICF = 57%
  - Percentage of ECF
    %ECF = (ECF/ TBW) x 100%
    %ECF = (19.62/45.84) x 100%
    %ECF = 43%

The results of data collection analysis from 10 volunteers to be shown on the graph and linearity graph between H^2/Z and intracellular fluid (ICF) and extracellular fluid (ECF) which can be seen in Table 4 and Figure 12 and 13.

Tabel 4 : Data device and analysis

No.	Height (cm)	Weight (kg)	Frequency (kHz)	Impedance (Ω)	Body Water (L)	TBW (L)	Persentage (%)	
							ICF	ECF
1	168	70	20	937	19.62	45.84	57	43
			75	682	26.22			
2	164	74	20	989	17.91	41.15	56	44
			75	741	23.24			
3	165	55	20	1463	12.88	27.92	54	46
			75	1222	15.03			
4	157	46	20	1293	13.15	28.74	54	46
			75	1061	15.59			
5	160	52	20	1420	13.90	29.24	52	48
			75	1268	15.33			
6	178	77	20	939	21.74	45.40	52	48
			75	856	23.66			
7	170	58	20	1224	14.23	36.95	61	39
			75	723	22.72			
8	171	62	20	1294	15.22	35.06	57	43
			75	959	19.84			
9	172	76	20	945	20.32	46.00	56	44
			75	731	25.68			
10	167	79	20	937	19.41	46.68	58	42
			75	646	27.26			

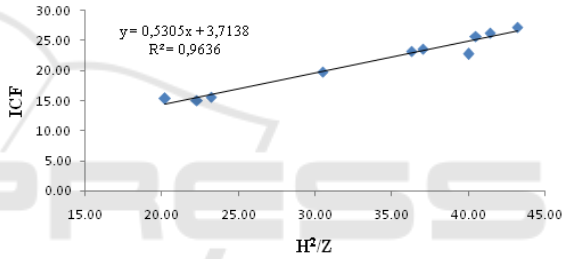

Figure 12 : Graph of linearity between H^2/Z and ICF

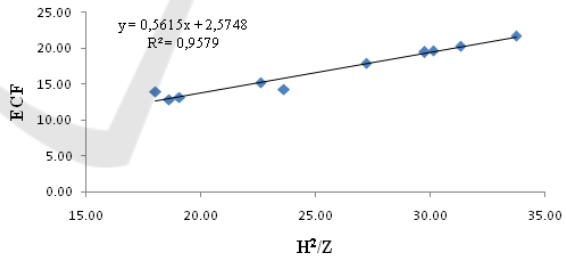

Figure 13 : Graph of linearity between H^2/Z and ECF

4 CONCLUSIONS

The dual frequency bioelectrical impedance as diagnostic candidate for dengue fever patient can be used to monitor the percentage of intracellular fluid (ICF) and extracellular liquid (ECF). The intracellular fluid (ICF) was obtained from the measurement of total body impedance value at high frequency (75 kHz) with linearity of R^2 = 0.9636 and extracellular liquid (ECF) was obtained from the result of measuring total body impedance value

at low frequency (20 kHz) with linearity of R^2 = 0.9579.

REFERENCES

Deen J et al. 2006. *The WHO Dengue Classification and Case Definitions : Time for a Reassessment*. Lancet., 368 : 170 – 173.

Ginanjar, Genis. 2008. *Demam Berdarah, a Survival Guide*. Yogyakarta : B – First.

Hoffer et al. 1969. *Correlation of Whole – Body Impedance with Total Body Water Volume*. J. Appl. Physiol, 27, 531 – 534.

Ibrahim et al. 2005. *A Novel Approach to Classify Risk in Dengue Hemorrhagic Fever* (DHF) *Using Bioelectrical Impedance Analysis* (BIA). IEEE Transactions On Instrumentation And Measurement, Vol. 54, No. 1.

Ibrahim et al. 2007. *A New Approach to Classify Risk in Dengue Infection Using Bioelectrical Impedance Analysis*. Dengue Bulletin – Volume 31.

Jaffrin et al. 2008. *Body Fluid Volumes Measurements by Impedance : A Review of Bioimpedance Spectroscopy* (BIS) *and Bioimpedance Analysis* (BIA) *Methods*. Med. Eng. Phys., 30, 1257 – 1269.

Moissl et al. 2006. *Body Fluid Volume Determination via Body Composition Spectroscopy in Health and Disease*. Physiol. Meas., 27, 921 – 933.

World Health Organization. 2009. *Dengue : Guidelines for Diagnosis, Treatment, Prevention and Control.* Switzerland : WHO Press.