International Journal of Electronics & Informatics

ORIGINAL ARTICLE

Microcontroller Based Automatic Switching Types Multi-frequency Electrical Impedance Spectroscopy(EIS) System For Early Detection of Breast Cancer

Shekh Md Mahmudul Islam and Md Adnan Kiber

ISSN: 2186-0114
http://www.IJEI.org

ARTICLE HISTORY

Received: 14 June, 2013
Revised: 12 October, 2013
Accepted: 7 October, 2013

Published online:

8 December, 2013

Vol. 2 , No. 2, 2013

Abstract

Breast Cancer is among the top five causes of cancer death and topmost cause among women worldwide. The early diagnosis through simple, non-invasive and inexpensive screening can provide great deal of aid especially for the poor people of Bangladesh. Making diagnostics measurement available to the widely geographically spread population in developing countries is a challenge which is unlikely to be met by the technology used in the west. Multi-frequency Electrical Impedance Spectroscopy is quite attractive in this context as the instrumentation is relatively simple and there is no known health hazard. Electrical Impedance Spectroscopy has been the subject of quite intensive research in breast cancer screening for about 10 years. EIS is a medical imaging technique in which image of the conductivity or permittivity of part of the object is inferred from the surface of the electrical measurement through a set of electrodes. Tissue impedance spectroscopy involves injection of constant current into tissues at different frequencies and measurement of voltage gradients. Automatic switching system is needed for the reliability of the EIS system and automatic switching between electrodes are implemented using digitally controlled analogue switch (MC14551B) and the sequence of switching is controlled by locally available microcontroller ATmega8.This paper focuses on the instrumentation of microcontroller based automatic switching type EIS system for early detection of breast cancer. In this research work EIS system has been designed using function generator,Howland V/I converter, automatic switching system using digitally controlled analogue switch(Mc14551B) and the sequence of switching is controlled by microcontroller ATmega8,instrumentation amplifier and Butterworth bandpass filter. In our previous research work the automatic switching between electrodes has not been done but in this research work automatic switching has been implemented using Arduino board microcontroller and Arduino board has been designed. The performance of designed EIS system each section is found to be satisfactory and measurement on resistive components gave an error of 2.2% which indicates that proposed system can be used for breast cancer screening trials.

Keywords: *Electrical Impedance Spectroscopy, Multi-frequency, Microcontroller, Instrumentation*

I. INTRODUCTION

BREAST CANCER is one of the most common cancers and leading cause of cancer death among women worldwide [1][2].Breast cancer incidence is increasing over the year with more than 1 million reported each year[3].In addition to that an average 37,300 women died globally in conjunction to the disease[2][4].As there is no cancer registry system in Bangladesh so we do not have accurate data on this. Like other developed countries the number of patients is increasing day by day in Bangladesh too. The most common form of screening system available to

AUTHORS INFO

*Author 1*Shekh Md Mahmudul Islam*
e-mail: mahmud_apececadet@yahoo.com
Address: Department of Applied Physics, Electronics & Communication Engineering, University of Dhaka

Author 2 Md Adnan Kiber
e-mail:ma_kiber@yahoo.com
Address:APECE,DU

*Corresponding author
e-mail: mahmud_apececadet@yahoo.com

the mass people is mammography. Mammography is the process of using low dose x-ray to examine human breast. Mammography is an expensive and health hazardous breast screening procedure. Electrical Impedance Spectroscopy has been the subject of quite intensive research for about 10 years. EIS is a medical imaging technique in which image of the conductivity or permittivity of part of the body is inferred from surface electrical measurement. There are several advantages of EIS over other medical imaging techniques.

1. It is comparatively cheap technique over other imaging techniques.
2. There are no known health hazards attached to it.
3. Data can be collected very rapidly so that change in function can be measured.
4. By making spectral measurement tissue characterization can be made.
5. Long term monitoring physical function is possible.

Considering the advantages of the technique and the socio-economic condition of the poor people in Bangladesh EIS could be an alternative to expensive medical imaging technique like Mammography and MRI.If they found positive in low cost, non-invasive EIS then they could go for expensive medical imaging technique like Mammography, MRI etc. The human body is made of tiny building block called Cells. Usually the body creates normal and healthy cells. But if a cell changes into an abnormal sometimes harmful form, it can divide quickly over and over without dying, making multiple copies of it. When this happens a tumour or abnormal body cells grouped together in the form of a mass or lump can start to form and grow. Breast Cancer is a kind of tumour that develops in the cells of a person breast. A tumour can form anywhere in body. Someone has cancer when those abnormal cells will not stop growing. Sometimes breast cancer spreads other parts of the body, like the bones the liver elsewhere.

Human body shows a unique response when subjected to signal of varying frequencies. Each of the body part has significant frequency dependent responsive behaviour. At a particular frequency, there are large differences between the impedances of organs. The behaviour can be utilized to detect the presence of any abnormality residing inside any particular organ if the original behaviour is known. Bioimpedance is a term used to describe the response of a living organism to externally applied electric current or voltage. It is a measure of the opposition to the flow of electric current through the tissues. The bioimpedance variation of normal cell and cancerous cell is the key to diagnosis.

It is expected that there will change in bioimpedance between normal and cancerous tissue which is the base of Electrical Impedance Spectroscopy for early breast cancer screening. Our designed low-cost, non-invasive Electrical Impedance Spectroscopy (EIS) System works in the frequency range of 10 KHz to 100 KHz as the high frequency ICs are not available in the local market of Bangladesh. For voiding the complexity of the design a four electrode EIS system has been designed and implemented. There are different methods for bioimpedance measurement.

1. Neighbouring method: The current is injected through neighbouring electrode like 1,2 electrodes(Fig1)
2. Cross method: The current is injected through the cross electrode like 1,3(Fig1)
3. Opposite method: The current is injected through 1,8 electrode(Fig1)

Because of better sensitivity in this research work, we have used neighbouring method for bioimpedance measurement.

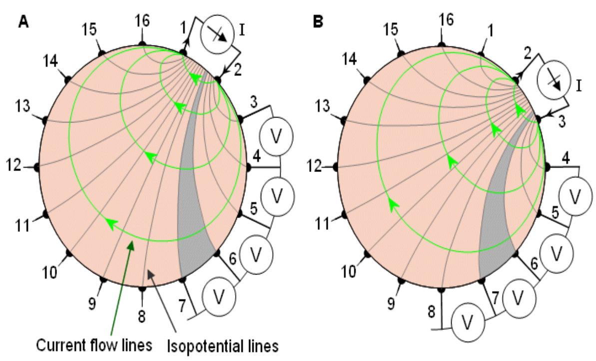


Fig. 1. Neighbouring method of impedance data collection

Switching between the electrodes during one profile of bioimpedance calculation is needed. In this research work, EIS automatic switching system (digitally controlled analogue switch MC14551B) has been implemented using local available high performance, low power 8-bit AVR ATmega8 microcontroller. An Arduino board has been designed. Arduino is an open source single board microcontroller descendent of the open source wiring platform, designed to make the process of using electronics in multidisciplinary projects more available. An Arduino board consists of 8-bit Atmel AVR microcontroller with complimentary components to facilitate programming in-corporation to other circuits. Most board consists of 5V linear regulator and 16 MHz crystal oscillator. All boards are programmed over RS-232 serial connection. This paper focuses on the instrumentation part of microcontroller based automatic switching based EIS system and measurement performance of each section.

II. SYSTEM DESIGN

The design requirements which are based on the published variation of tissue impedance with frequency [5][6][7][8] are taken into consideration. Ten measurement frequencies in the range 10 KHz-100 KHz are taken into consideration. The specification for the designed microcontroller based EIS system is given below:

TABLE I. Specification For Microcontroller based Multi-frequency EIS system

Features	Specifications
Excitation Frequency	10 KHz-100 KHz
Drive Current	1 mA(p-p)
Current Drive output impedance	< 50 KΩ

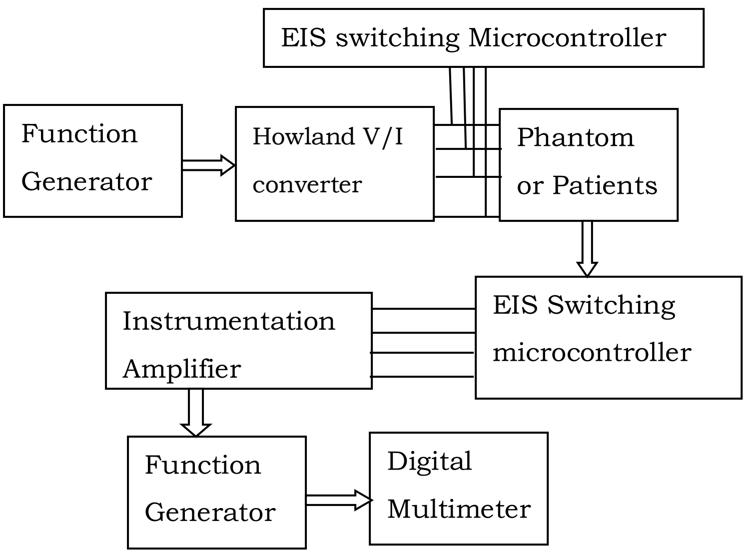


Fig. 2. Block diagram of designed EIS system

The designed block diagram shown in Fig.2 describes the system operation and design methods. The signal generated of various frequencies controlled externally. The amplitude can be altered externally by varying values of components. The voltage-to-current converter converts the voltage signal to low amplitude current signal. The current is pushed through separate electrodes and injected to the organ under test and generated response is collected through two other electrodes. When current is injected between 1, 2 electrode and then voltage is measured in 3,4 electrode and sequence is repeated by switching to complete one profile of bioimpedance data. A digitally controlled analogue switch MC14551B has been used for switching action and the sequence of switching is controlled by locally available microcontroller ATmega8.A program is designed and implemented for automatic sequence of switching between the electrodes have been done using microcontroller. The recipient electrode feed the signal to a wideband high gain, high CMRR instrumentation amplifier. The signal is then feed to a bandpass filter and then finally RMS voltage is measured using digital Multimeter.

Current Drive Section:

In tetraploar EIS measurement, an alternating current of constant amplitude is injected into the body through two electrodes and the resulting voltage across two other electrodes is measured. To maintain the amplitude of the applied current constant, a current source with high output impedance is required. The current drive section is designed by cascading Function generator using XR2206 IC and Howland V/I converter.XR-2206 is a monolithic function generator which is locally available IC in Bangladesh. By varying the value of resistors or capacitors different frequencies signals can be generated. The generated signal has excellent temperature stability, wide sweep range and adjustable amplitude

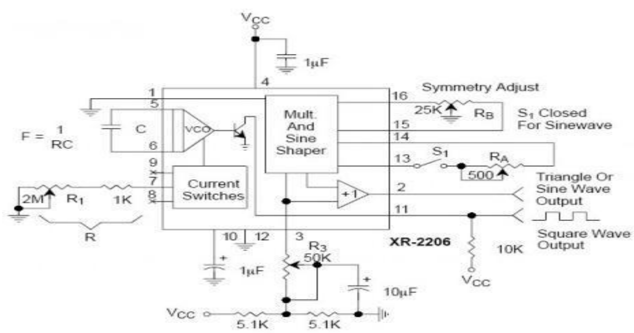


Fig. 3. Working circuit diagram of sine wave generation

Enhanced Howland V/I Converter:

High frequency low level current is to be injected to the human body which needs a constant current source as bioimpedance varies on diseased condition as well as one person to another. Voltage-to-current converter or constant current source is an essential part of the multi-frequency EIS system. The structure of the enhanced howland circuit is very simple and its performances is predictable [9][10].An Enhanced V/I converter is designed which to keep the current level constant(1 mA).The performances of Enhanced Howland and basic howland circuit is measured by practical and simulation study both. Because of better performance Enhanced Howland circuit has been used in this research work.

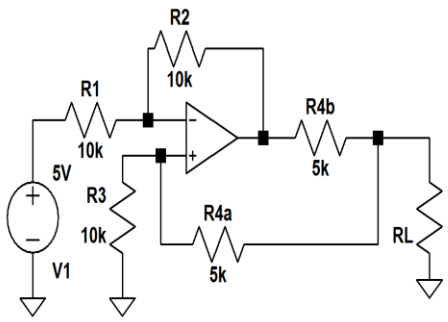


Fig. 4. Enhanced Howland V/I Converter

EIS automatic switching:
The four electrode EIS needed two tetraploar measurements for each frequency, where the direction of current drive and voltage measuring electrode pairs were altered [11].The injection of current by using two electrodes is controlled by using microcontroller. Here the function of the microcontroller is to select the two electrodes from four electrodes. The two electrodes will be selected in a rotating manner for current injection like 1, 2; 2, 3; 3, 4; 4, 1 and similarly for the voltage measurement the rotation of selection would be just opposite like 4,1;3,4;2,3;1,2.In this research work, we have used AVR ATMega8 which is low power CMOS 8-bit microcontroller. We have used Arduino board for microcontroller programming. Arduino is an open source single board microcontroller descendent of the open source wiring platform, designed to make the process of using electronics in multidisciplinary projects more accessible.

In the first measurement (Fig 5) switch **X** was connected to current drive terminal and switch **Y** was connected to terminal 3 so that electrodes **A** and **B** were used to inject current whilst electrodes **C** and **D** were used to measure the resulting voltage. .In the second measurement switch X was connected to terminal 2 and switch **Y** was connected to terminal 4,so current was injected through electrodes **A** and **C** and the voltage was measured across electrodes.

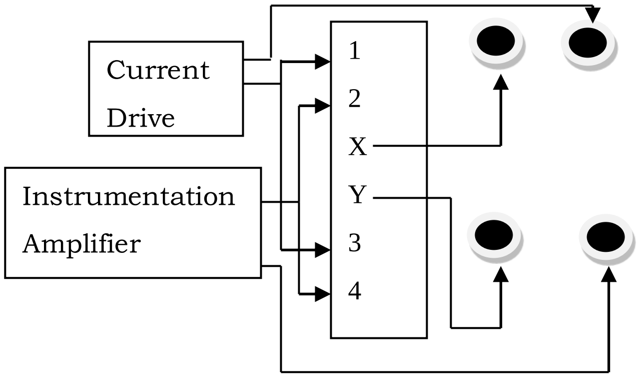


Fig. 5. EIS switching system using microcontroller (ATmega8) and Arduino board used in this research work. **B** and **D**.A digitally controlled analogue switch MC14551B was used for switching and the sequence was controlled by microcontroller AT mega8

Instrumentation Amplifier:
An instrumentation amplifier is used to amplify the voltage signal from the body minimizing any common mode signal. The instrumentation amplifier shown in figure consists of two stages. The first stage consists of non-inverting amplifiers and the next section is difference *amplifier.* The overall gain of the designed instrumentation amplifier is 50 and the common mode rejection ratio is 63 dB and 50 dB at 10 KHz and 100 KHz respectively.

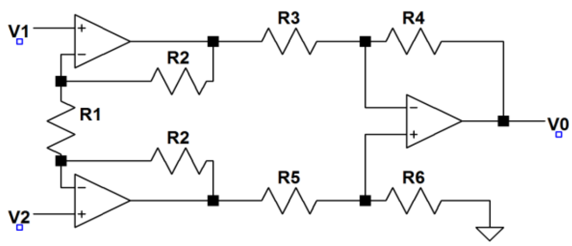


Fig. 6. An instrumentation amplifier of overall gain 50 and CMRR of 63dB using TL074 IC

Butterworth bandpass filter:

To improve signal-to-noise ratio, a Butterworth bandpass filter has been designed which have a voltage gain of 1 and a pass band from 10 KHz to 100 KHz. Butterworth filter has flat pass band characteristics. A high frequency TL074 op-amp has been utilized for the wide band characteristics

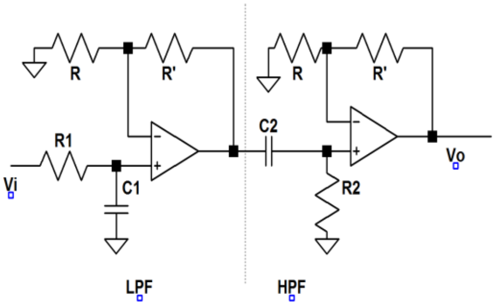


Fig. 7. Butterworth Bandpass filter using TL074 IC

Arduino Board Design:

Arduino is an open source electronics prototype platform based on flexible, easy to use hardware and software. It is intended anyone any one for artist, designer and engineers. Most of the research work is done by this package now a day. In this research work an Arduino board has been designed and implemented by soldering it together. Our designed Arduino board consists of 5V linear regulator and a 16 MHz oscillator. The board is programmed over RS-232 serial connection.

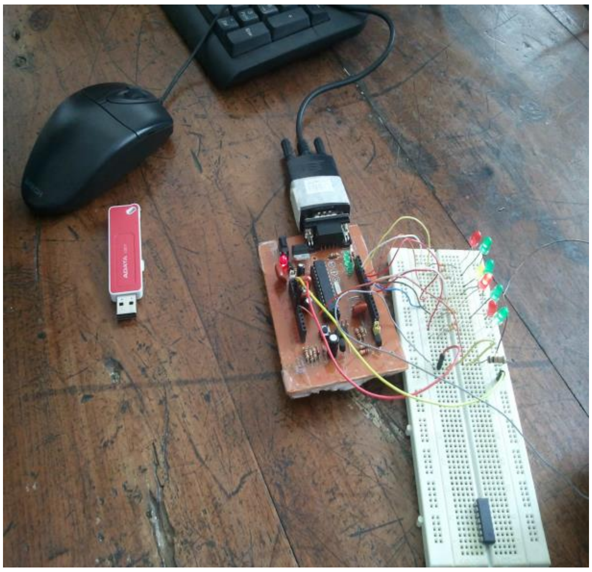


Fig. 8. An Arduino board designed and PC Connected using RS232 interface

Programs of Microcontroller:

The Arduino IDE is a cross platform application written in JAVA and is derived from IDE for the processing program language. The program has been implemented using delay time almost 1 millisecond.

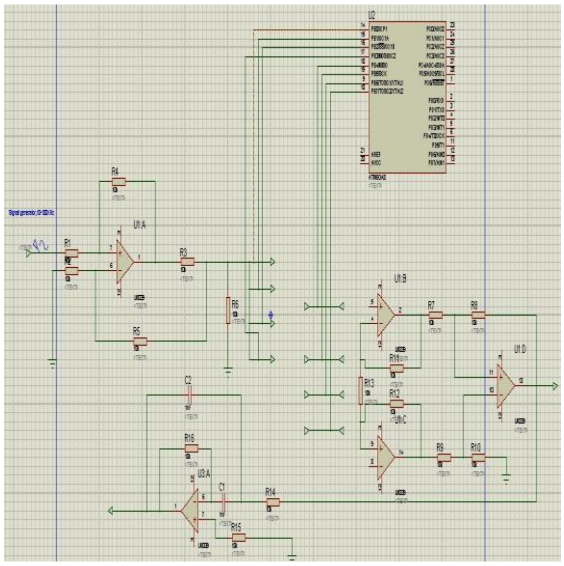
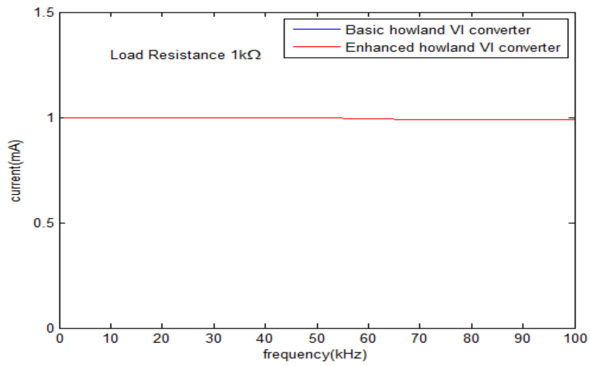


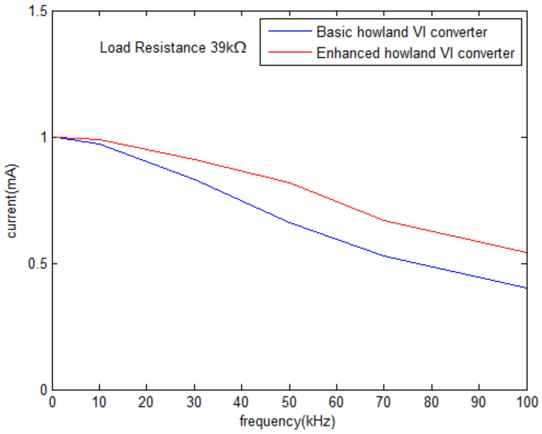
Fig. 9. Schematic diagram of Designed EIS System

III. RESULTS

In this research work, we have measured the performances of each and every section of the designed EIS system. The current drive section consists of function generator and Enhanced Howland circuit. The performances of current drive section is largely depends on the performances V/I converter. We have used two different types of V/I converter one is Basic Howland circuit [11] and another is Enhanced Howland Circuit. The performances are measured using the specification [5] [6] [7] [8].Simulation and practical studies on the comparative performances of Basic Howland and Enhanced Howland circuits are given below:



(a)



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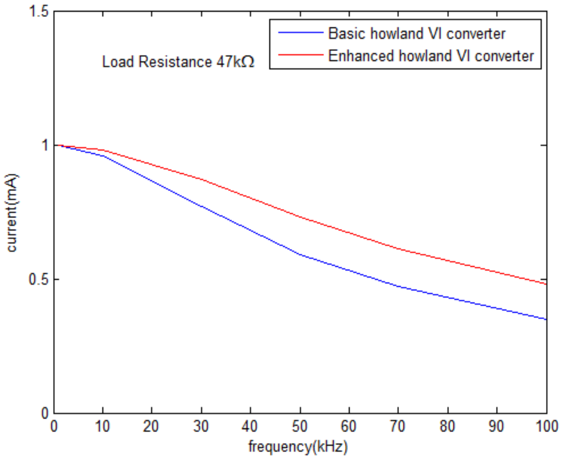
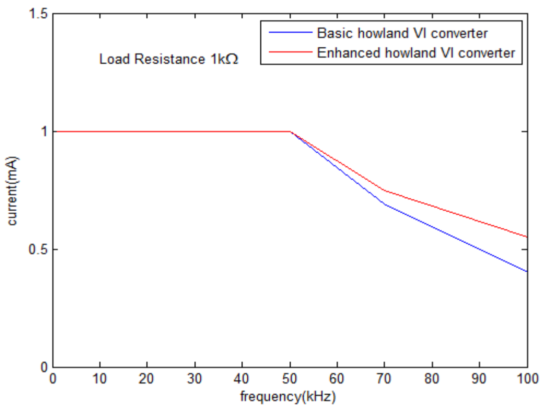
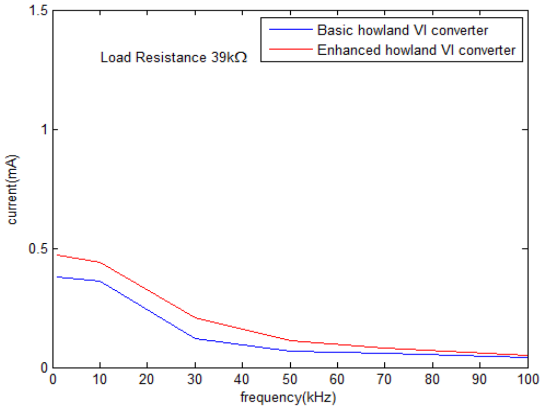


(c)

Fig. 10. Simulation (Multisim software) study of the performances of Basic Howland and Enhanced Howland voltage-to-current converters. (a) Load resistance 1 kΩ (b) load resistance 39 KΩ (c) load resistance 47 kΩ. Results should be clear and concise.



(a)



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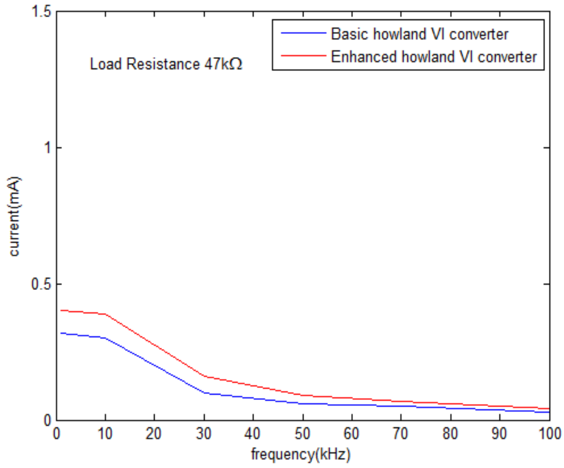

(c)

Fig. 11.Practical study of performances of Enhanced Howland and Basic Howland V/I converter (a)load resistance 1 kΩ (b) load resistance 39 kΩ (c) load resistance 47 kΩ.

As the signal frequency and the load resistance increase the designed current level (1 mA) decreases. The performance of Enhanced Howland circuit supersedes the performance of basic howland circuit in all of the cases. So, in our research work we have used Enhanced Howland circuit for its better performances. The output impedance of Enhanced Howland circuit was measured to be 387 KΩ for 10 KHz signal and 48 KΩ for 1024 KHz signal. The current level (1 mA p-p) of the designed Enhanced Howland circuit remains constant up to 5KΩ before going into saturation.

The common mode rejection ratio (CMRR) of the instrumentation amplifier is 63 dB and 37 dB at 10 KHz and 1024 KHz respectively. The performance of Butterworth bandpass filter remains constant and its upper cut-off frequency and lower cut-off frequency or bandwidth has been verified using different signal frequencies. After implementing the program in a microcontroller LED has been used for verification of the switching section and it implements the proposed designed programs in an Arduino board.

To test the accuracy and reproducibility of the measurement system, current was injected through various known resistor chains and corresponding impedance was measured at each frequency. Each measurement was repeated ten times to study the measurements reproducibility. The resistor (Fig. 10) R was set to 1KΩ to simulate the Electrode-tissue contact impedance. If the applied known resistance was **R_{known}** and the resistance measured by multi-frequency EIS system was **$R_{measured}$**, then the percentage of error was calculated using equation(1)

$$\text{Error} = \frac{\text{Rknown} - \text{Rmeasured}}{Rknown} \times 100\%$$

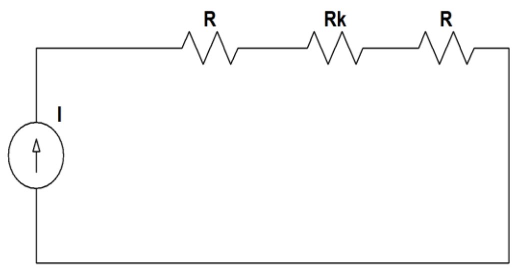

Fig. 12. Resistive Phantom to study the accuracy of the designed EIS system

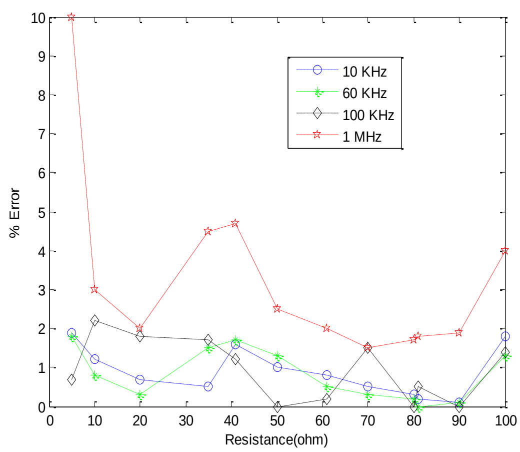

Fig. 13.Percentage of measurement error at three different frequencies for varying load resistances.

Figure 11 shows the percentage of error in the measured resistance value against the actual resistance values at four different frequencies. If the result at 1024 KHz were ignored, the measurement error was well below 2.2%.

IV. Conclusions

Multi-frequency Electrical Impedance Spectroscopy system has been designed and implemented using locally available inexpensive circuit elements so that biomedical engineers in the field can maintain it. One of the important subsystem of the designed EIS system is automatic switching between electrodes and automatic switching has been implemented using digitally controlled analogue switch MC14551B and the sequence of switching has been controlled automatically by locally available microcontroller ATmega8.An Arduino board has been built for the proposed EIS system. The performance of individual section of the proposed EIS system has been measured .As the electrical current method is new to doctor and patients and there is no permission from Bangladesh Medical Research Council so we could not take any practical bioimpedance data. Resistive phantom studies are done and the measurement error is less than 2.2%.The performance described in this paper is adequate to undertake filed trials in early breast cancer screening of our low cost designed EIS system

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