New system for early breast cancer detection by Electrical impedance spectroscopy

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***Abstract*:-** Breast Cancer is among the top five causes of cancer death and the topmost cause among women worldwide. representing 16% of all female cancers[3]. breast cancer is diagnosed in 1 in 8 women[3]. Worldwide, it is estimated that more than 1.5 million women are diagnosed with breast cancer every year, and $2.4B was spent on breast cancer screening in 2009[3].The Multifrequency Electrical Impedance Spectroscopy (EIS)early diagnosis through simple, non-invasive and inexpensive screening can provide great deal of aids. In our project we are focusing on the design and construction of the device ,Working with software which installed on computer connected with that device, we use an Arduino UNO board with built-in microcontroller of (ATmega328p). It based EIS system has been designed and implemented using function generator (LM5401), Howland V/I design by different value of resistors, and Amplifiers, electrodes; Electrical impedance scanning (EIS) maps are a measure of the electrical properties of an object made through surface measurements through automatic switching system using microcontroller, Instrumentation amplifier and Butterworth bandpass filter. On other hand our software focusing on the generated signal from the electric circuit and then processes it to specifics if there is any abnormal state or existing tumor on breast according to the changes of measured electrical bioimpedance.

***Key-Words*:-** Breast Cancer, Electrical Impedance Spectroscopy EIS, Microcontroller, Instrumentation amplifier, Enhance Howland converter.

1 Introduction

Breast cancer is an insidious disease that may be present and may be develope over many years with out signs or symptoms of any kind.

In 2012, the worldwide incidence of breast cancer was estimated to be 1.7 million (11.9%)[11]. In our country -Yemen- there are no accurate official statistics for the number of breast cancer cases that increases day by day. The early diagnosis through simple, non-invasive and inexpensive can provide a great aids for patients who have this kind of cancer. Until now no suitable methods have been avaliable. Most techniques are too invasive, too expensive and not accurate enough because they relay on assumptions which are not valid.

Multi-frecuancy electrical impedance spectroscopy (EIS)[1][10] is the non-invasive medical techniqe in which perform the condactivity of body is inferred from surface electrical measurment. However, this technique baised on sensing the changes in the electrical impedance of the body by measuring the resistance of the body to an alternating current and the impedance is measuerd at multiple frequencies between 10KHz and up to 200KHz. At low frequencies the curent is conducted by extracellular water (ECW) because cell walls and tissue interfaces act as conductors. At higher frequencies this capasitive effect is lost and the current will pass through all conducting material. Theoretically, this methode makes it possible to measure ECW as well as intraculler water (ICW). There are several advantages of EIS over other medical technique that is, It requires low-cost instrumentation, easily applicable in practice, enable on-line monitoring, Data can be collected very rapidly so that change in function can be measured, By making Spectral measurement tissue characterization can be made and Long term monitoring physical function is possible.

In this study we will discuss the charactristics and methods of the system.These methods are howland, bioimpedance measurement, EIS switching and Instrumentation with butterwoth bandpass filtering that used with EIS technique illustrated with diagrams. Finally EIS environment system connected with serial communication and show test results in GUI interfaces.

2 Related Work

Research and development issues in Elictrical impedance cover a range of topics, as EIT which is being investigated in the field of breast imaging as an alternative/complementary technique to mammography and magnetic resonance imaging (MRI) for breast cancer detection. The low specificity of mammography [13] and of MRI [14] result in a relatively high rate of false positive screenings, with high distress for patients and cost for healthcare structures. Development of alternative imaging techniques for this indication would be desirable due to the shortcomings of the existing methods: ionizing radiation in mammography and the risk of inducing nephrogenic systemic fibrosis (NSF) in patients with decreased renal function by administering the contrast agent used in breast MRI,Gadolinium. , using electrical impedance tomography (EIT). This technique enables visualization of the spatial distribution of conductivity in the human body; several research groups work on EIT systems for breast imaging (see, for example, Tunstall et al 1998, Wtorek et al 1999). Application of this method to breast cancer detection requires special design of the measuring system and image reconstruction algorithm, as imaging of a three-dimensional distribution of conductivity is required. The resolution of the EIT system falls significantly with increasing distance from measuring electrodes, and traditional EIT measurement schemes are unsuitable for mammography because of this. A large number of electrodes, which are required to provide acceptable resolution of the system, leads to enormous increases in computation time for image reconstruction.Also Experimental studies have shown that significant changes occur in the electrical properties of breast cancer tissue compared to the surrounding normal tissue. This phenomenon motivated studies on cancer detection using electrical impedance techniques[15]. Some evidence has been found that malignant breast tumors have lower electrical impedance than surrounding normal tissues. This observation has led to the proposal that electrical impedance could be used as an indicator for breast cancer detection. However, the separation of malignant tumors from benign lesions based on impedance measurements needs further investigation [16]. There are no prospective clinical studies demonstrating the clinical utility of electrical impedance scanning (EIS) in distinguishing benign from malignant breast lesions, either in place of or as an adjunct to mammography or magnetic resonance imaging[18]. An assessment of technologies for breast cancer screening and diagnosis conducted by the Institute of Medicine of the National Academy of Sciences (2001) concluded that clinical data suggest the technology [EIS] could play a role in breast cancer detection, but more study is needed to define a role in relation to existing technologies[17].

Application of this method to breast cancer detection requires a special design of the measuring system and image reconstruction algorithm, as imaging of a three-dimensional distribution of conductivity is required. The breast cancer detection device, electric impedance mammography machine designed and developed by the Institute of Radio-Engineering and Electronics of the Russian Academy of Science and is being currently marketed by TD-SIM Technika of Yaroslavl city, Russia. It is a 3D EIT system which consists of a compact of electrodes positioned over the tissues being measured, two additional electrodes placed remotely from the array of electrodes, a source of alternating current (AC), a means to measure potential difference and computing means to reconstruct and visualize the conductivity distribution as stack of tomography images . Utilizing this new system, a complete 3-D diagnostic test takes 20 seconds for each breast totaling to 40 seconds for both the breasts. Seven tomographic image slices appear on a computer monitor within 40seconds at depths of 0.4cm to 4.6cm to detect and isolate tumors. These coronal images include tissue near the chest wall. This reconstruction process can be compared to CT or PET scanning but without radiation of any kind and at a significantly lower cost[19,2]. In section 3, we illustrate the framework of main idea of Electrical Impedance spectroscopy and Project Subsystems.

3 Frame Work Of The System

3.1 Specification

The requirement EIS measures in terms of electrical and biological, probably varies of tissue impedance to measure the output impedance of the current drive section, different load resistances were driven by the current at each frequency into range 10 KHz to 200 KHz. And 5V the input voltage (source volts).The current source was designed to deliver 500 µA (p-p) and was measured to deliver this into a load resistance up to 10 KΩ . The output impedance of the current source was measured to be greater than 60 Ω for normal breast phantom model.

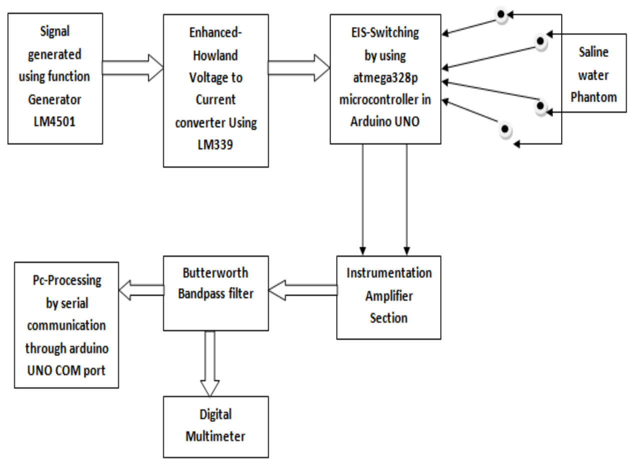

Fig.1 Block Diagram of Designed multi-frequency EIS

The signal generated of various frequencies are controlled externally by using local available LM5401 Function Generator, Generate sine (sinusoidal function) signal with Multi frequencies from 10 KHz to 200 KHz and 5V and input voltage(source volts). The voltage-to-current converter converts the voltage signal to deliver 500 µA current signal. The current is pushed through two separate electrodes and injected to the body of human When current is injected between two electrode and then voltage is measured in other two electrodes. This sequence operation is repeated by microcontroller . it's work as automatic switching to Scanning the deep surface in body, and send the voltage to instrumentation to measure the bioimpedanc and enhancement and filtering signal. It consists of an Improved Howland Current Source controlled by voltage, a load voltage sensing scheme through a discrete 3-opamp instrumentation amplifier, a phase and quadrature demodulation setup through analog multipliers, and digitization and processing of the signals using a digital benchtop multimeter. The end seand the signal after enhance and filter to the microcontroller to send the computer.

3.2 Schematic diagram of EIS System

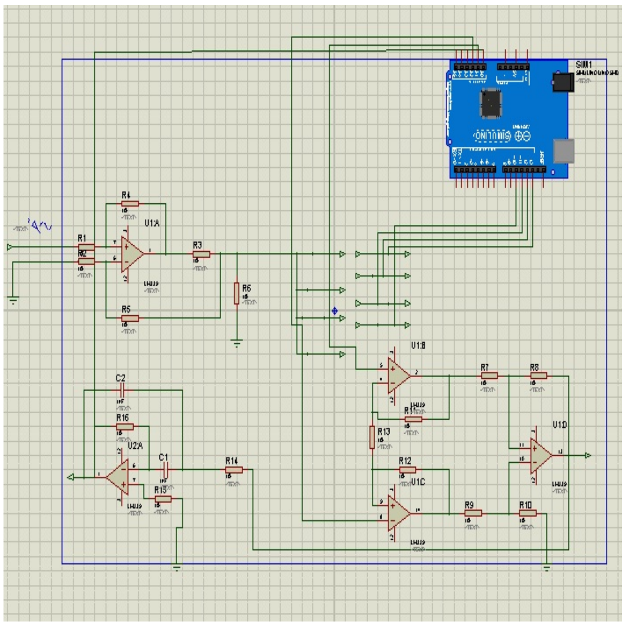

Fig.2 Schematic diagram

3.3 The Enhanced Howland Current Source

The Howland Current Source is a well known and widely used circuit for realizing voltage controlled current sources for loads with one end connected to the ground. Several variants of the original circuit which are often referred to as the modified Howland circuits have already been proposed.

The circuit discussed in this work is one of these circuits. The essential features of the original Howland circuit have been preserved[7].

The structure of enhanced Howland circuit is very simple and its performance is predictable .Hence, the enhanced Howland circuit is employed here for the circuit of current source. The schematic diagram of enhanced Howland circuit is shown in Figure 4.[8].

Measuring the output current from the howland circuit by using multimeter connected in series with resistance load 10Kohms, then the output current could equals 717 microamperes in ideal case.

3.4 Bioimpedance measurement method

Four-Electrode method, also referred as tetrapolar or Kelvin method; it is the most common way to measure the impedance. The four electrode methods is the best choice for soft tissue but it is not error free. It can be found that the error sources limit the useful bandwidth of the measurement probe. Two electrode s are attached to the body through which the alternating electric current enters

the body[4]. Two detection electrodes are also attached to the body within the linear location of these two current electrodes, and the values of resistance and reactance are measured across these two detection electrodes. The length of the conductor is technically the linear distance between the two detection electrodes[4]. In adults, there is a minimal allowed distance between current and detection electrodes of about 4 to 5 cm to avoid electrical interference[4].

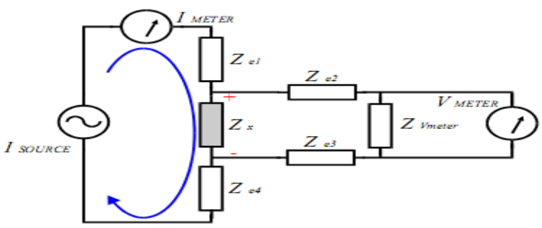

Fig.4 Schematic representation of four-electrodes method

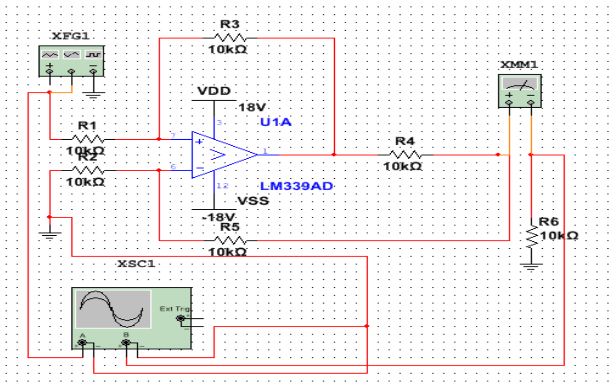

Fig.3 Multisim Simulation of Enhanced Howland Current-to-Voltage Converter

An rectangular shaped Plastic phantom has been built with a height of 7inches and 5inches width; so that saline water can be entered into it. Three layers of plastic phantom are used for measuring impedances. we experimented the system on EIS phantom models.

A rectangular shaped Plastic Phantom The width of the first, second and third layers are respectively equals inches. Four screws with wires are used as electrodesand all electrodes are equally spaced. The layer wise phantom studies are done and the measured curves are given below in Fig.5. A plastic pot with 2.3inches is also used for measuring impedances. When it is inserted in the cylindrical shaped phantom then variation of impedances is also detected as in Fig.6.

Fig.5

Fig.6

3.5 EIS Automatic Switching system

Our EIS System needed automatic switching between it's four electrodes to make two electrodes for current drive and the other for voltage drive and repeat the

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Permutations between the four electrodes, and it should be automatically; for that purpose we used atmega328 microcontroller with Arduino UNO which is programmed with Arduino C.

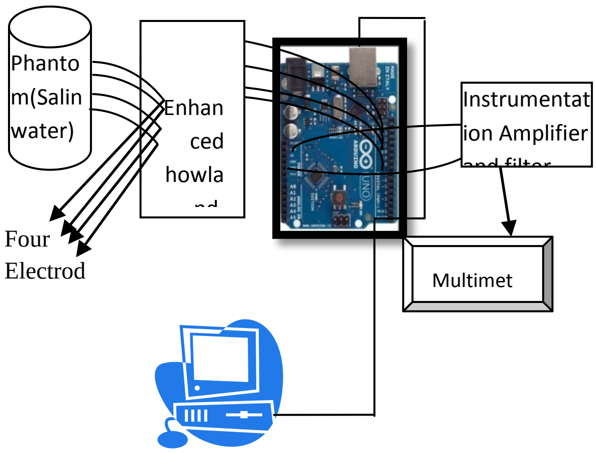

Fig.7 block diagram of EIS Switching System Connection

As illustrated above the four electrodes connected to the arduino uno over enhance howland system then it transfer over arduino uno to instrumentation amplifier and filtering System(control the switching automatically by microcontroller on arduino uno), the measured output voltage of the whole system from pin1 after filtering connected to the A0 arduino uno pin to transfer the output signal to the PC for processing using USB serial connection.

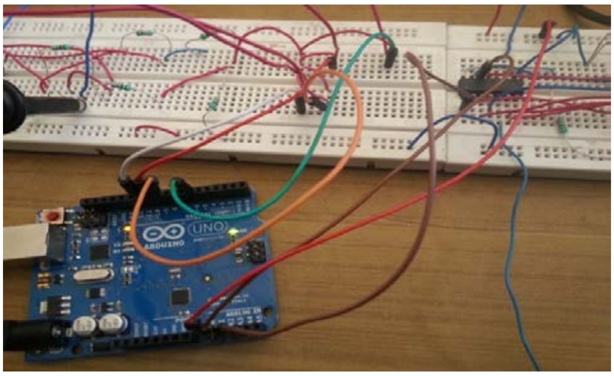

Fig.8 EIS Switching system

6.3 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[7]. The Instrumentation Amplifier (IA) resembles the differential amplifier, with the main difference that the inputs are buffered by two Op Amps. Besides that, it is designed for low DC offset, low offset drift with temperature, low input bias currents and high common-mode rejection ratio. These qualities makethe IA very useful in analog circuit design, in precision applications and in sensor signal processing.

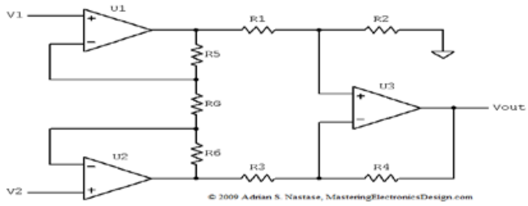

Fig.9 Instrumentation amplifier

7.3 Butterworth band pass filter

Butterworth bandpass filter To improve signal-to-noise ratio(Signal-to-noise ratio is a measure used in science and engineering that compares the level of a desired signal to the level of background noise.), a Butterworth bandpass filter has been designed which have a voltage gain of 1 and a bandpass from 10 KHz to 200 KHz in our proposed EIS system. Butterworth filter has flat pass band characteristics[1]. A high frequency LM339 op-amp has been utilized for the wide band characteristics.

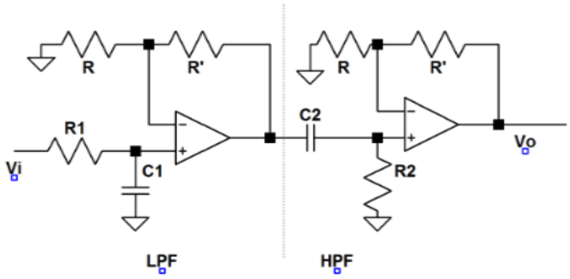

Fig.10 Butterworth passband filter.

The Butterworth filter is a type of signal processing filter designed to have as flat a frequency response as possible in the passband. It is also referred to as a maximally flat magnitude filter. It has no ripple in the pass band or the stop band, and because of this is sometimes called a maximally flat filter. Frequency Response From Butterworth passband filter.

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8.3 Serial communication

Communicating via serial ports requires three things: computers with serial ports, a cable or wireless interface that provides a physical link between the ports, and programming to manage the communications.

9.3 Graphical user Interface

the designed user interface by WPF c# programming language used to analyze the received data by a serial communication and then clarify the changes in impedance of the phantom whereas the plastic pot with a saline water inserted to it or not , this interface clarify that the designed EIS can measure the impedance under different layers as the phantom designed to simulate the breast tissue with it's internal layer , the graphical User interface also developed to be able to detect early breast cancer for real patients in near future so the patients information and diagnosis of him can stored in database and be comparable with each test operation

4 Results

We applied EIS system on a plastic phantom to measure the output impedance of the current drive section, different load resistances were driven by the current at each frequency. The current source was designed to deliver 500 µA (p-p) and was measured to deliver this into a load resistance up to 10 KΩ . The common mode rejection ratio(CMRR) of the instrumentation amplifier used to amplify the voltage signal.

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.

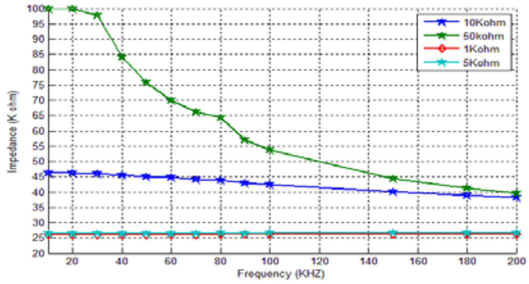

Fig.11 Impedances Vs Frequencies under different load resistors

Simulation and practical studies on the comparative performances of Enhanced Howland circuits are given below:

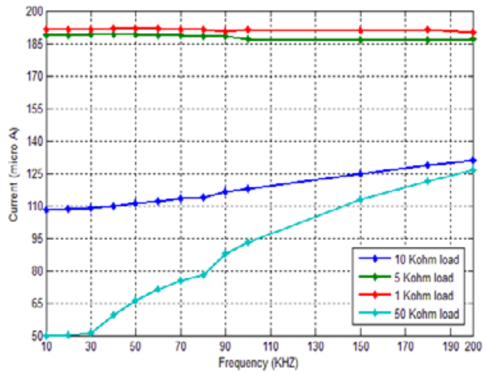

Fig.12 Frequency characteristics of the Impedance of normal and cancerous breast tissue

The typical theoretical injected current should be lower than 1 mA that is safe for human body; in practical we got 200µA over 200 KHz with 1KΩ resistance load as illustrated above, in our research work we have choose 10KΩ,5KΩ as resistance load to get the most appropriate value of the injected current. The output voltage of the instrumentation

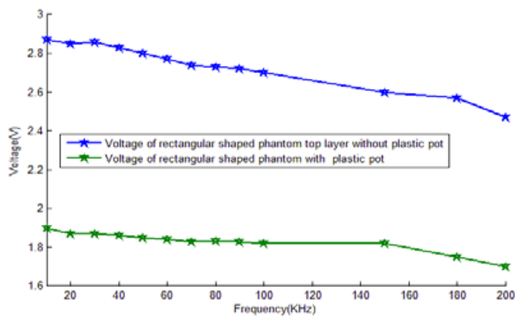

Fig.13 Voltage vs. frequency curves of a top level rectangular shaped plastic phantom

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amplifier could not be greater than 5V in order to avoid exceeding the input voltage range of the ADC of the microcontroller ATMEGA328p built in with Arduino UNO. However, if the instrumentation amplifier output was less than 250 mV, then the differentiator at 10 KHz was too small to be detected by the voltage comparator.

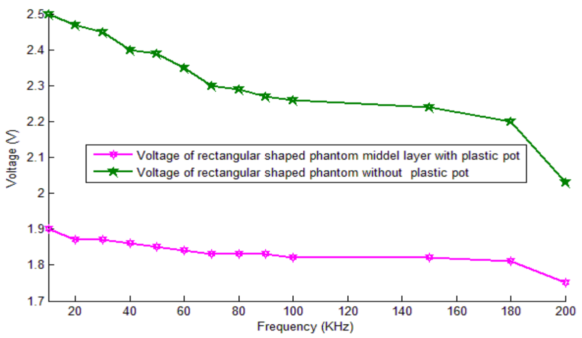

Fig.14 Voltage vs. frequency curves of a middle level rectangular shaped plastic phantom

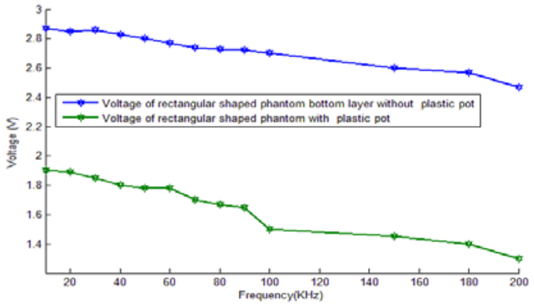

Fig.15 Voltage vs. frequency curves of a bottom level rectangular shaped plastic phantom

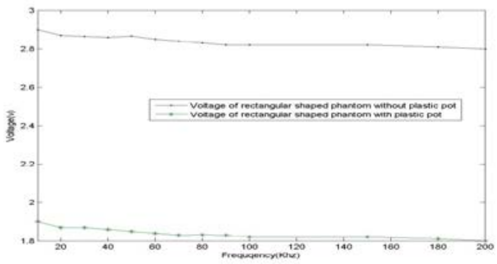

Fig.16 Voltage vs. frequency curves of a rectangular shaped plastic phantom when current is injected between 1,2 electrode and voltage is measured 3,4 electrodes also when current is injected between 2,3 and voltage is measured 4,1 electrodes also when current is injected between 3,4 electrode and voltage is measured 1,2 electrode and when current I injected between 4,1 electrode and voltage is measured between 2,3 electrodes.

To test the accuracy and reproducibility of the measurement system, current was injected through cole-cole phantom model and the corresponding impedance was measured at each frequency. Each measurement was repeated many times to study the measurements reproducibility. The designed EIS system was also tested for capacitive loads by replacing the load resistor R in Howland circuit with a Cole-Cole model phantom (74 Ω in parallel with 24Ω in series with 4.7 nF) Figure7.1 shows the Cole-Cole phantom and figure7.2 shows the measured impedance value against Calculated impedance value for this phantom and the maximum error is 1.9%.

$$\text{Error} = \frac{R_{\text{theoritical}} - R_{\text{measured}}}{R_{\text{theoritical}}} * 100\%$$

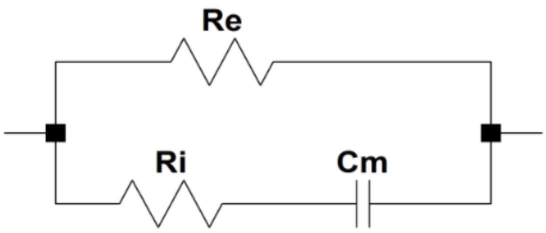

Fig.17 Capacitive Cole-Cole Phantom

5 Conclusion

The Multi frequency electrical impedance spectroscopy that we have been implemented it using a available electronic element in yemen and few of the elements imported from abroad .the automatic switching and the sequence of electrodes were controlled by Arduino UNO with a built in Atmega328p microcontroller programmed by Arduino C programming language .The measurements of EIS tested by measuring the output voltage of rectangular phantom with and without another smaller phantom inserted inside the rectangular phantom . The performance of individual section of the proposed EIS system has been measured using Cole-Cole model and the measurement error is less than 1.7%. no any practical bioimpedance data collected from real patients as there is no permission from Yemen ministry of health . Measurements on resistive, Cole-Cole and rectangular shaped phantom gives a hint that the proposed EIS system is a proper to undertake field trials in breast cancer screening for early detection.

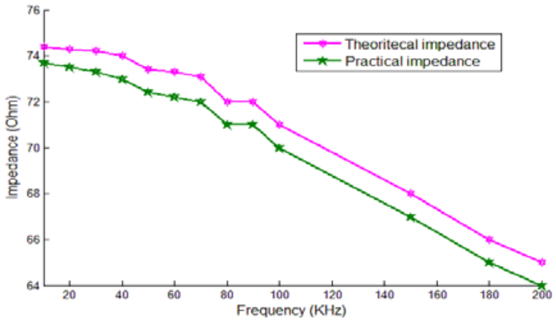

Fig.18 Comparison between measured impedance and calculated impedance of a Cole-Cole Phantom.

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