Instrumentation of Tissue Impedance Measurement System and the Detection of Cancer Tissue based on Capacitance Spectra of the Prostate

Naheed Hossain, Md. Taslim Reza, AdnanQuaium, Mohammad Rakibul Islam, Kazi Khairul Islam

Abstract— It is very important to identify the malignant tissue in the early stage to prevent cancer. Tissue impedance variation is a significant characteristic to identify the malignant tissue from suspected cancer tissue. We analyze the impedance of a set of practically measured malignant and benign tissue, collected from prostate of a number of patients. A simple tissue equivalent circuit is proposed and also found that for the applied supply frequency from 300 kHz to 500 kHz, a considerable deviation of tissue capacitance is found. We also discuss about the tissue impedance measurement system and the electronics setup used for this kind of measurement.

Index Terms— Impedance measurement, 4 lead system, 2 lead system, prostate cancer, impedance spectrum, tissue equivalent circuit, tissue capacitance.

1 Introduction

THE word "Cancer" means a group of diseases that are characterized by unrestrained cellular development. It It refers to cellular intrusion into neighboring tissues and may turn into metastasise if not treated at early stage. The most widely diagnosed malignancy in males is prostate cancer. Peripheral zone of the gland is the place where prostate cancers are generally found. It constitutes a dense arrangement of cancerous epithelial cells commonly in small form, penetrating glands with a symmetrical decrease in stromal volume [2]. B. Lee *et al.* [3] used tissue bioimpedance to differentiate between the diseases because morphological differences between normal and malignant prostate tissue are present and sensitivity of electrical impedance spectra to cellular structure was known. Bioimpedance is one of the properties referred to a tissue's resistance when electrical current flows in the tissue. It also means the ability of tissue to store electrical charges. Bioimpedance normally depends on spacing of cells, cellular density and size, and the components of the extracellular matrix (ECM). Differences between the malignant and benign tissue impedance of can be a distinguishing criteria for pathological procedures for cancer detection [1]. Actually, it was shown by Skourou *et al.* [4] that when there is tumor, the tissue impedance may be more sensible than conventional imaging techniques, such as computed tomography (CT) and ultrasound imaging. Normal and neo-plastic condition has been differentiated by using electrical impedance of tissue in analyses of cervical, breast, skin, and bladder tissues [5][6][7][8]. It was shown in the Lee study [3] that the resistance of malignant tissue was higher than normal tissue but the capacitive differences between normal and malignant tissues were not discussed.

In this paper we studied the nature of the prostate tumor tissue impedance from a practically found data set. A tissue equivalent circuit is also proposed by which capacitance of the tissue can be calculated from that data set of various tumor tissues for a band of applied frequency. Experimental result suggests that for a range of frequency the normal and malignant tissues have significant deviation of capacitance to which helps to differentiate between them. We also discuss about the use of different lead systems to measure tissue impedance and suggest the effective one for that purpose.

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2 Ease of Use

2.1 4 Lead System for Impedance Measurement

Bio-impedance measurement can be done by passing current through the tissue. This tissue impedance produces voltage and that can be measured by proper instrumentation. Tissue impedance measurement device can be similar to a temperature measurement system (TMS). Sensor impedance, used in TMS, varies for the variation of temperature where the tissue impedance varies for the different characteristics of the tissues. A very simple configuration of impedance measurement system is shown in Fig. 1. There is a current source connected to the tissue and voltmeter connected to the current leads [9].

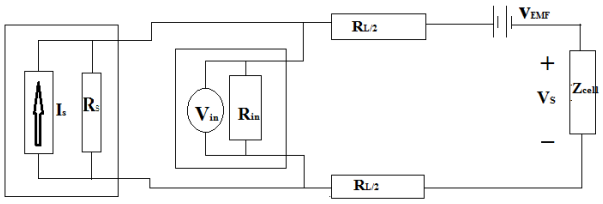

Fig. 1. 2 Lead impedance measurements

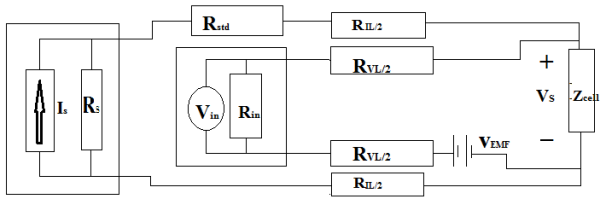

Fig. 2. 4 Lead impedance measurements

The current source (I_s) has a shunt resistance Rs in parallel. It can be represented as an ideal current source**.** The voltmeter (V_{in}) is a digital multi-meter (DMM) with an input impedance (R_{in}). It can be modeled as an ideal voltmeter.

Generally the very common origin of error in a 2-lead impedance measurement is the lead wires resistance. These lead wires connect the current source to the impedance source.2-lead measurement system has an effect of lead resistance also. 4-lead impedance measurement (Fig. 2) can be used to eliminate the effects of lead resistance. Between these four leads, two of them are from positive and negative voltage supply source. These two leads are used to measure the impedance voltage leads and to eliminate the effect of lead resistance. For this kind of voltage measurement the voltmeter needs very small current (in range of pico-amperes or less) so that the voltage drops in the voltage leads are extremely small. The resistive drop in the current leads is not measured in this scheme. It means that the voltage drop in $R_{IL/2}$ is out of voltmeter measurement. That is why the measurement scheme works fine. Other two leads are connected to positive and negative port of the current source.

2.2 Choice of Needle and Operating Frequency

The effectiveness of a tissue impedance measuring system, particularly at low frequencies, is evaluated mostly by the electrode-tissue, or electrode-electrolyte, interface impedance [10]. Unexpected impedance can be taken as the source of noise signal. Matching and reduction of electrode-tissue impedance solve the unexpected impedance problem to some extent. One of the effective ways to reduce the electrode-tissue impedance is to increase the conductance of the electrode-tissue interface. Conductance increased by enlarging the electrode surface because the interface conductance is directly related to the surface area of electrode. We can expand the electrode surface area or the surface roughness. Each of these techniques will reduce interface impedance at low frequencies [11].

At frequencies below 100Hz, the electrode-electrolyte interface impedance involves vital tissue impedance measurement errors. The capacitive coupling of the wires is strongly visible at frequencies beyond 100 kHz [11]. That is why the frequency band might be limited between 100 Hz to 100 kHz but not obvious.

3 Data Analysis and Equivalent Circuit

The impedances of normal and malignant tissues, for differ ent supply frequencies, are taken from a well mentioned practical experiment. Table 1.1 shows the tissue impedance values both for normal and malignant tissues. Five *ex vivo* prostates were taken and impedance spectra were measured in the operating room immediately following radical prostatectomy.

It is observed that, there are overlaps in the impedance ranges for malignant and normal tissue considerably between patients. It makes difficult for the selection of a suitable impedance threshold to differentia normal and malignant tissue. This overlap creates from inter patient variability in the impedance of tissues. It happens mostly due to instinctive variability between patients and inconsistency within different locations of the prostate.

Study shows that, the region for impedance measurement within the prostate for all patients are not same. In the experiment, tissue impedance measurements were taken on the contra lateral lobe of the prostate and the position of the tumor for each patient were symmetric. There is much smaller variation in the measurements of malignant and normal tissue and each of these were confirmed by histology of the acquired data. A simple equivalent circuit has a resistance and a capacitance in parallel, mentioned in Fig. 3. We propose this simple model for better understanding of the tissue impedance change with respect to variation of supply frequencies. Here *R* is taken as 10 kΩ/m.

Based on the experimental results, we propose that equivalent circuit. This equivalent circuit may differ for different structure of tissue. From the equivalent circuit Z_{tissue} can be derived as:

$$Z = X_c * R / (X_c + R) \quad (1)$$

Tissue reactance, $X_C = 1/2\pi f$, where f is the supply frequency. From (1) we can derive the equivalent capacitance, *C* as:

$$C = ((1/Z_{tissue}) - (1/R)) * 1/2\pi f \quad (2)$$

Z_{tissue} is taken from the experiment [1] and capacitance is calculated by (2) for different supply frequencies and also plotted by using MATLAB software.

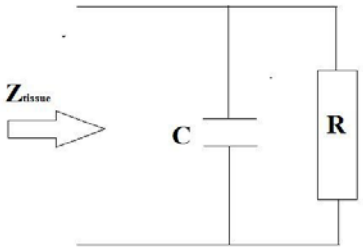

Fig. 3. Simple tissue equivalent circuit

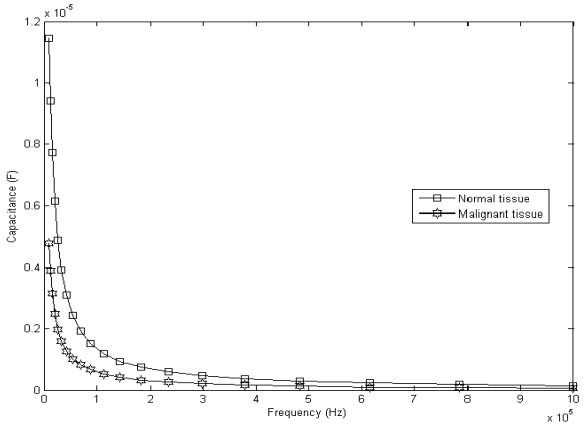

Fig. 4. Capacitance spectra of normal and malignant tissue

4 RESULT

We plot the capacitance of normal and malignant tissue by using (1), which is shown in fig. 4. Here, we use the minimum value of impedance from table 1.1 and supply frequencies from 10 kHz to 1 MHz. In fig. 4, we observe that the capacitance spectra of normal and malignant tissue give significant variation for a band of supply frequency. Capacitance for both normal and malignant tissue seems almost constant from the frequency 300 kHz to above, in case of the proposed tissue equivalent circuit. It shows that our proposed simple equivalent circuit will work for the supply frequency more than 300 kHz. However, there is a clear deviation of the capacitance spectra between normal and malignant tissue for the frequency band of 300 kHz to 500 kHz, which is shown in
Fig. 5. This significant deviation of capacitance will help to distinguish malignant tissue from normal tissue.

TABLE 1
CHANGE OF IMPEDANCE WITH RESPECT TO FREQUENCY

Frequency(kHz)	Impedance For normal	Impedance for malignant
10	1.39-5.88	3.33-4.17
12.7	1.35-5.71	3.22-4.00
16.2	1.33-5.56	3.12-3.92
20.7	1.27-5.40	3.08-3.84
26.4	1.25-5.32	3.03-3.77
33.6	1.23-5.26	2.99-3.70
42.8	1.21-5.21	2.94-3.64
54.6	1.20-5.15	2.86-3.57
69.5	1.20-5.13	2.78-3.51
88.6	1.19-5.10	2.70-3.47
113	1.18-5.05	2.67-3.45
144	1.18-5.00	2.63-3.42
183	1.17-4.88	2.62-3.40
234	1.16-4.76	2.60-3.39
298	1.15-4.65	2.58-3.38
379	1.14-4.55	2.56-3.37
483	1.13-4.44	2.56-3.36
616	1.12-4.35	2.53-3.34
785	1.10-4.26	2.51-3.33
1000	1.09-4.17	2.50-3.32

5 DISCUSSION

To eliminate the effects of lead resistance error, 4-lead measurement can be used. As a result, better measurement accuracy is possible. This system is used for highest accuracy of rapidly changing input. Very minor impedance changes can also be calculated by this system. Since capacitance of the normal and malignant tissue is nearly constant between the ranges of 300 kHz to 500 kHz with a significant difference between each other, it is better to record the tissue impedance within that range to identify the malignant tissue.

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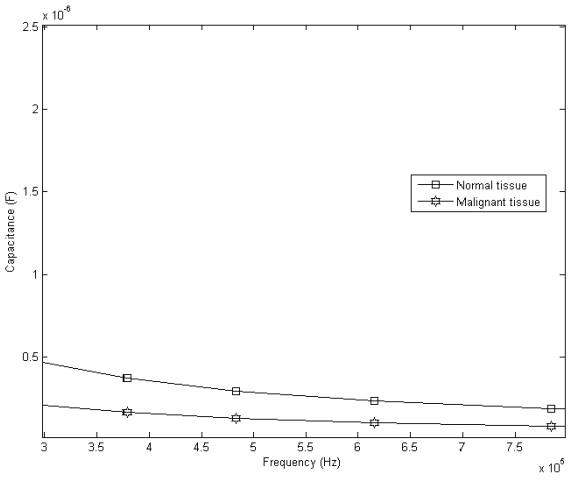

Fig. 5. Variation of capacitance of normal and malignant tissue starting from 300 kHz to 500 kHz

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