ELECTRICAL IMPEDANCE ANALYSIS OF BIOPSY SPECIMENS TO DISTINGUISH HEALTHY AND CANCEROUS BREAST TISSUES

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ABSTRACT

One of the most common cancer types in the world is breast cancer. Screening and diagnostic methods like mammography, ultrasound or magnetic resonance imaging are not enough for all clinical situations to conclude about the exact nature of the lesions found in the breast tissue. Therefore, physicians need biopsy as an invasive procedure. The aim of this study was to investigate the electrical impedance of abnormal and normal breast tissue, in order to find a new method, for reliable, non-invasive detection of breast cancer. For this purpose, breast tissues taken from five patients were provided Bezmialem Vakif University Faculty of Medicine Department of General Surgery, and impedance measurements have been done at the Pathology Department of the same university. Impedances of healthy and tumoral tissues for each patient were measured. Analysis of impedance values has shown significant difference between healthy and tumoral tissues

***Index Terms*—** Electrical impedance spectroscopy, breast cancer, Bode plot, breast tissue, biopsy

1. INTRODUCTION

Breast cancer is a cancer originating from breast tissue and it can be divided into two classes as ductal carcinomas and lobular carcinomas, those are originating from ducts and lobules respectively [1]. This type of cancer is the most common malignant tumor among women in the western world [2, 3]. Breast cancer can occur in males as well.

Early diagnosis increases the success of treatment, while delayed diagnosis leads to an increase in the risk of death [2]. For diagnosis of breast cancer, mammography, magnetic resonance imaging and ultrasound are frequently used. Though these techniques can help to detect the pathologic lesions found in the breast tissues, determination of the tumor as benign or malignant remains weak.

Mammography is the most widely used method for breast cancer diagnosis in clinical practice [4, 5]. Ultrasound is used for discrimination of cystic lesions from solid ones [6]. Besides the cost of breast magnetic resonance imaging, it's sensitivity and specificity ranges from 94-100% and 37-97%, respectively [7]. Therefore, these imaging techniques are usually used as an adjunct to mammography.

Biopsy procedure is time-consuming process and requires specialized staff in the biopsy. This situation leads to delays in diagnosis. In addition, this procedure involves an invasive surgical operation, therefore causes physical and emotional damage in patients [7]. Due to such disadvantages, researchers are working on alternative methods such as computer aided image processing techniques and electrical impedance analysis.

Electrical impedance, indicated by Z, is combination of resistance (real part) and reactance (imaginary part).

$$Z = R + jX \tag{1}$$

Each cell consists of intracellular fluid and surrounding cell membrane. There are ion channels on this membrane that provides ion balance of intracellular and extracellular fluids. These fluids consisting of water and electrolytes are resistive. As can be seen in Fig. 1, ion channels on the membrane shows capacitive and resistive properties [8]. Thus, a living tissue exhibits electrical impedance under alternative current [9]. In the 10 Hz-10 kHz frequency range, impedance is mainly affected by the ionic structure around the cell. However, in the 10 kHz-10 MHz frequency range, impedance is affected by membranes as well [7][10]. These properties are not used in clinical applications but obtained results are promising.

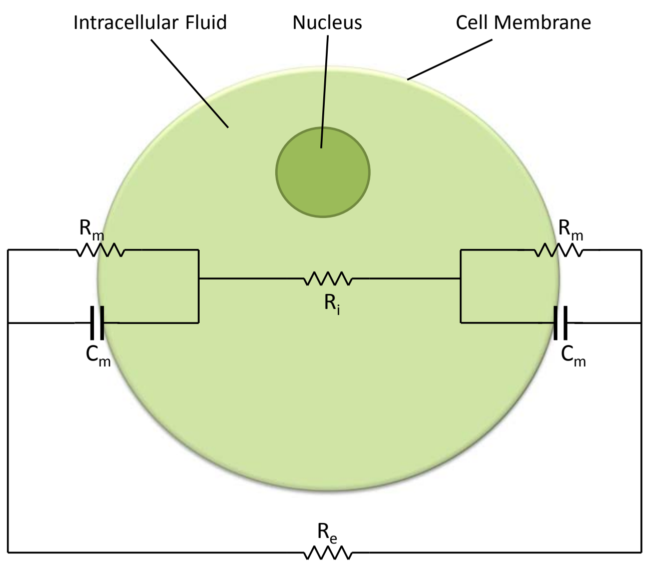

Fig. 1 Electrically equivalent model of a single cell. Re: Exracellular fluid resistance, Ri: Intracellular fluid resistance, Rm: Cell membrane resistance, Cm: Cell membrane capacitance

It is shown for the first time that cancerous and healthy tissues show different impedance properties in the frequency range between 20 kHz - 100 MHz, by Frick and Morse in 1920 [11]. Morimoto et al. found significant differences between malignant and benign tissue at 200 kHz in vivo electrical impedance measurements [12]. In another study conducted by Stelter, [13] significant differences of electrical impedance values between cancerous and healthy tissue at frequencies ranging from 100 Hz to 10 MHz was found.

In this study, electrical impedance values of the breast at frequencies between 10 Hz and 100 kHz were measured and Bode Plot differences of healthy fibroglandular and tumoral tissues were analyzed.

The rest of the paper is organized as follows: The data and methods which are used to analyze the Electrical Impedance Measurements are described in the section of the Material and Methods. Experimental results, discussion and evaluation are given in Results-Discussion and Conclusion section, respectively.

2. MATERIAL AND METHODS

For this study, an Ethical Approval Document is obtained from Bezmialem Vakif University (No: 71306642/050-01-04/ 59). Patients were informed, and their written consents were acquired.

Our dataset consist of healthy fibroglandular and tumoral tissues taken from five patients. After excision of the tissues, pathologic analysis and preparation for impedance measurements were performed simultaneously. Tumoral tissues declared as invasive breast carcinoma and normal healthy tissues were determined. Impedance measurements are performed in a specifically prepared laboratory at most one hour after the surgery by researchers at Institute of Biomedical Engineering, Fatih University, Şükrü Okkesim and İmran Yıldırım. Laboratory temperature was kept at 24 C°. The measurements were analyzed by drawing Bode diagrams. Bode diagrams are commonly used for tissue impedance analysis [14].

Bode plots are the most widely used graph to display a transfer function of a linear, time-invariant system versus frequency. Using a Bode plot, frequency response of a system can be easily evaluated. A bode plot compose of two parts, namely magnitude and phase parts. A Bode magnitude plot part represent the magnitude of the frequency response gain and Bode phase plot represent the frequency response phase shift.

Measurements were performed with CH Instruments 6005D impedance analysis device at frequencies ranging from 10 to 100,000 Hz, at 48 different frequency points increasing geometrically. Applied voltage was 5 mV during the test. Two seconds of quiet time is applied between different frequency measurements.

Two Au electrodes configuration was used to measure the electrical impedance (Fig. 2). Interelectrode distance was manually set as 2 mm as can be seen in Fig. 3.

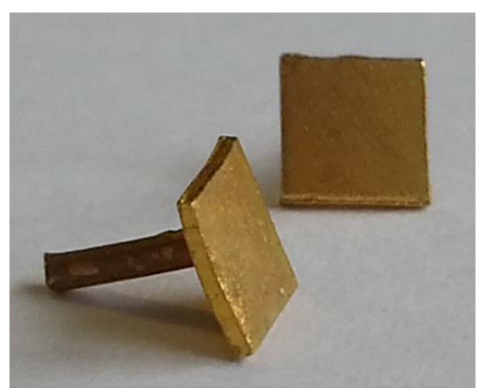

Fig. 2: The gold electrodes

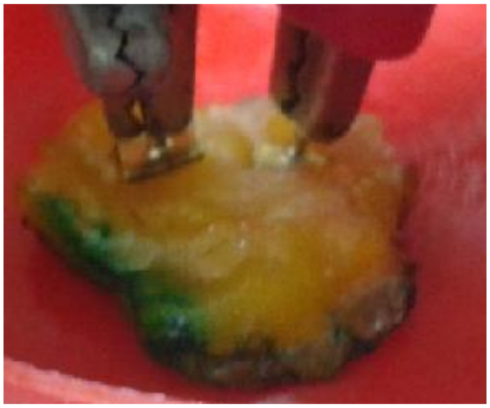

Fig. 3: Positions of the electrodes during the measurement

All the data processing and statistical analysis was carried out using in-house programs developed under MATLAB R2009b Software (MathWorks Inc., Natick MA, USA).

3. RESULTS

In this study, electrical impedance measurements are performed and differences between breast cancer and healthy tissues are investigated. Measurements are shown as Bode plots after processing with MATLAB.

TABLE I.

MEAN VALUES AND STANDARD DEVIATIONS OF ELECTRICAL IMPEDANCES AT FREQUENCY BANDS (H:HEALTHY T: CANCEROUS)

Freq.	Type		# 1	# 2	# 3	# 4	# 5
10-100 Hz	H	μ	0.576	2.46	7.52	0.247	0.208
		σ	0.129	0.171	0.428	0.00196	0.00538
	T	μ	0.239	0.616	0.261	0.199	0.204
		σ	0.00363	0.0202	0.00961	0.00314	0.00366
100-1000 Hz	H	μ	0.175	0.201	8.17	0.21	0.206
		σ	0.000338	0.00242	2.1	0.0011	0.00106
	T	μ	0.208	0.198	0.216	0.209	0.21
		σ	0.001	0.000589	0.00135	0.00197	0.0016
1-10 KHz	H	μ	0.217	0.224	0.854	0.207	0.207
		σ	0.0141	0.0142	0.628	0.0112	0.0119
	T	μ	0.214	0.205	0.205	0.203	0.208
		σ	0.0152	0.0127	0.011	0.0112	0.0113
10-100 KHz	H	μ	0.6	0.986	10.2	0.412	0.419
		σ	0.386	0.863	6.62	0.209	0.211
	T	μ	0.434	0.467	0.403	0.402	0.398
		σ	0.231	0.28	0.206	0.193	0.194

In table 1, impedance values are shown in terms of frequency bands. Mean and standard deviation values of each measurement from each patient are written in the table. Because of tissue size, some measurements are done single time compulsorily, and this affects standard deviation. Otherwise, standard deviations are quite small. This shows that measurements are consistent. As seen in table, 10-100 Hz and 10-100 KHz frequency bands are most distinctive between healthy and cancerous tissues. In other frequency bands, electrical impedance values are usually similar.

For patient 5, impedance values are not distinctive enough. This may be because of inadequate biopsy specimen.

In average Bode plot (see Fig. 4), y axis shows impedance values while x axis shows frequency values. Mean impedance graph of the 5 normal and 5 cancerous tissues are shown. As can be seen in figure, there is a difference between the healthy and cancerous tissue.

Especially below the 103Hz difference is clearer. In the range of, the 103Hz – 104Hz the difference between the healthy and cancerous tissue is decreased. As discussed in the introduction section, over the 104Hz impedance is affected by membranes and intracellular liquids. Thus, when the cancerous plot is examined in Fig. 4, it can be seen that cancerous tissue has different impedance values below the 103Hz and over the 104Hz due to the abnormalities of the cancerous cell's membranes and different ion concentrations. The obtained results are consistent with literature.

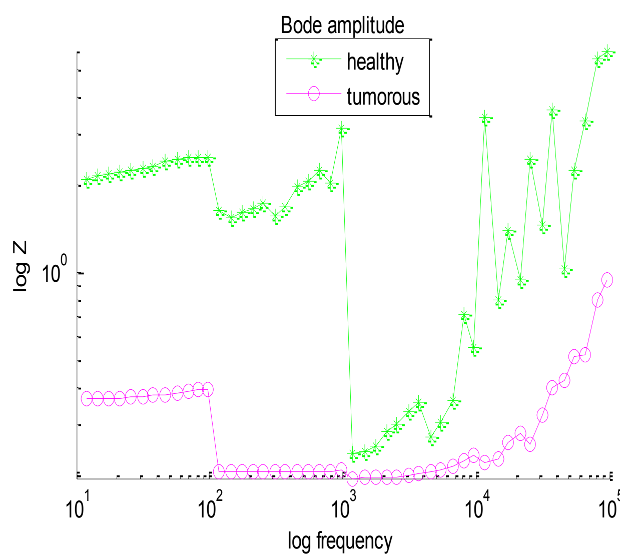

Fig. 4: Bode Diagram of Group Averages

Electrical impedance has been used for living tissue characterization for over 70 years and it has advantages like having low cost, ease of use and being minimally invasive. As a preliminary study, our aim was to measure the electrical impedance value of the cancerous and normal tissue in the range of 10 Hz – 100 KHz. Thanks to this study we acquired enough experience so that we can prepare a detailed project proposal to detect and classify the breast cancer.

4. CONCLUSIONS

Significant differences found between normal and pathological tissue with most of the studied parameters confirmed that impedance spectroscopy can be considered potentially suitable for breast cancer detection [15]. However biopsy procedure is done not just to detect the cancer tissue but also distinguish the subtype of cancer and to decide the treatment procedure. Therefore investigations should go on to add these properties.

In this study, the results are consistent with the literature. However, more accurate results will be obtained by getting more data. To get more accurate result the recruitment of the data is going on. We are also acquiring new data from non-cancer patients who have gone under reduction operations.

The device used in this study cannot measure the impedance value for over the 100 KHz. Another limitation of the device is that the probes cannot be fixed. We are working on a mechanism to fix the probes with a material that is resistant to our cleaning solvents.

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