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Review Article

Role of bioimpedance in cancer detection: A brief review

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ABSTRACT

Bioimpedance is a term, which describes the response of living organisms to an externally applied current. It is a measure of opposition to the flow of the applied current through tissues. The measurement of bioimpedance of a living organism is non-invasive method for assessing its composition. A bioimpedance signal can be used for characterizing the tissue. The electrical properties of tissue vary with different applied frequencies. Bioimpedance is a well-established method in detecting breast cancer, cervical cancer, prostate cancer, etc. The studies showed that there are significant differences in bioimpedance between normal tissues and cancerous tissue. With this view in mind narrative review article is written to deliberate role of bioimpedance in various malignancies of the body. We also discussed studies done on oral squamous cell carcinoma (OSCC) and realized the need for more studies especially on oral potentially malignant disorders and OSCC together. The role of bioimpedance in malignancies was searched in databases such as PUBMED and SCOPUS with no restriction to the date of publication. Articles published in English medical literature on OSCC have been selected for discussion.

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1. Introduction

Cellular membrane conductivity is well known phenomenon that is governed by the selective permeability of the membrane. The factors that contribute to cells' electric properties are intracellular ionic solution and proteins which can move in response to the applied fields.[1] Different tissue components at different frequencies control the bioimpedance of tissue. The conductivity and permittivity are frequency dependent and have complex values.[2] Specially in cancerous tissues, there is a change in bioimpedance, which is attributed to increased cellular water and salt content, altered membrane permeability, changed packing density, and orientation of cells.[3]

Thus study of bioelectrical properties of cells is an interesting area of research. This method of cell study has proved its potential in deriving data about the morphology and physiology of the cells.[4] This technology identifies and measures the non-biological parameters of the cells, which may bear the disease signature and can be used for noninvasive detection. A cell when subjected to an electric field offers resistance to the current flow. The insulating properties of the living cells are different under different applied frequency.[5] In order to sustain the required potential difference, the cells provides varying resistance and capacitance.[6] The cellular bioimpedance varies for different cellular activities in static and dynamic conditions. Thus the frequency response of the bioimpedance of the biological cells and/or tissues is greatly influenced by their physiological and chemical status and is different from individual to individual. Even the complex bioimpedance varies within tissues in a particular individual and also changes with the health status[7,8] depending on the physiochemical changes of the tissues.

Over the years bioimpedance has emerged as a better screening tool over the current screening methods since it is relatively low-cost, provides instant results, requires little training and therefore bioimpedance can be easily used in primary care centers or in developing countries, where multiple factors limit national screening programs. The potential advantages of real-time screening tests include: a reduction in patient anxiety; improved patient compliance; and the ability to repeat inadequate tests immediately.[9]

The present narrative article discusses the role of bioimpedance analysis in malignancies. Special emphasis has been given to the studies published on oral squamous cell carcinoma (OSCC).

2. Electrical properties of human tissue

Human tissue is a group of cells usually surrounded by tissue fluids. The intra cellular and extra-cellular fluids are basically resistive. It is well known that the electrical properties of biological tissues differ significantly depending on their structures. The membrane constituted by a thin lipid bilayer with leaky ion-channels is both capacitive and resistive. Since bioimpedance of human tissue contains both resistance and capacitance, it is complex and can be described by a serial representation, $Z = R + jX$, where Z is impedance; R, the resistance; and X is the reactance; or by a parallel representation $Y = G + jwC$, where $Y = 1/Z$ is admittance; G, the conductance; C, the capacitance; and w is the angular frequency. An alternative way to represent tissue admittance is by admittivity, expressed as $\sigma' = \sigma + sjw\varepsilon_0\varepsilon'$ where, σ' is tissue admittivity; σ, the tissue conductivity; ε', the tissue permittivity; and, ε_0 the dielectric constant of free space.

The frequency of applied electric field alters the electric properties of cells and tissues as seen from α-, β- and γ-dispersion.[10] The α-dispersion obtained at low frequencies (10 Hz–10 kHz) and is affected by the ionic environment surrounding the cells. The β-dispersion shows structure relaxation (10 kHz–10 MHz). At higher frequencies, the γ-dispersion is found to be related to water molecules. The α- and β-dispersion regions have more medical implications, since most changes occur in this range.[11] The bioimpedance of tissue also varies with temperature and time[12] and it is also anisotropic.[12,13]

3. Evolution of bioimpedance measurement devices

Abundant research reports are found in the literature on developing devices for bioimpedance measurement. In general, they can be classified into point bioimpedance measurement devices[14] and spectrum bioimpedance measurement devices.[15–17] An example of point bioimpedance measurement device, developed by Castelló et al., was a PC-based impedance and gain-phase analyzer, operating in the frequency range of 10 Hz to 200 kHz.[14] For spectrum bioimpedance measurement device, Yang and Wang developed a bioimpedance spectrometer working at the frequency range of 10 Hz to 1 MHz[15]; while a portable device for the measurement of bioimpedance spectroscopy, over a frequency range of 20 kHz to 1 MHz was developed by Yang et al.[16]

On the other hand, some researchers focused on designing bioimpedance imaging systems, which can generally be classified into transverse bioimpedance imaging systems[18–21] and planar bioimpedance imaging systems.[22] An example of transverse bioimpedance imaging systems, electrical resistivity tomography instrumentation was developed by Dickin and Wang.[20] This is followed by the development of a CMOS microelectrode array (an example of plantar bioimpedance imaging systems) by Chai et al.[22] Ching and Chen[23] constructed a 2-dimensional (2D) imaging system based on measurements of bioimpedance, for non-invasive detection and localization of pathological epithelial tissues.

Recently, Rodriguez et al.[24] prepared a bioimpedance sensor ASIC targeting a battery-free, miniature size, implantable device, which performs accurate 4-point complex impedance extraction in the frequency range from 2 kHz to 2 MHz. The ASIC is fabricated in 150 nm CMOS, has a size of 1.22 mm × 1.22 mm and consumes 165 μA from a 1.8 V power supply. The ASIC is embedded in a prototype, which communicates with, and is powered by an external reader device through inductive coupling.