Diagnostic Potential of Electrical Bio-Impedance for Skin and Oral Mucosa

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Abstract: Depending on the frequency range, Electrical Bio-Impedance (EBI) spectra of skin reflect the hydration of the stratum corneum, experimental irritative and allergic reactions, skin barrier properties, and alterations due to some diseases. For oral mucosa, the degree of keratinization is an important factor. Baseline values differ while reactions are reflected in a manner similar to skin. Patterns of indices can discriminate between different types of irritative reactions, possibly discriminate irritative reactions from allergic ones as well as differentiating some diseases. The sensitivity is high, and quantification of alterations below the visual threshold are possible non-invasively.

INTRODUCTION

The Cole-equation [1] has been used frequently for extraction of Cole-parameters by curve-fitting. The Cole-parameters can be associated with structures such as cell membranes, and intracellular and extracellular volume conductors. The Cole-equation provides an adequate fit to measured data from most tissues in a limited frequency range, but is not a good model for heterogeneous structures such as intact skin or intact mucous membranes [2]. Three major dispersions in biological tissue (the α-, β- and γ-dispersions) have been defined by Schwan [3]. A comprehensive technical and historical critical review has been compiled by Foster and Schwan [4]. For intact skin and intact mucous membranes, the α- and β-dispersions are not well separated, which makes curve-fitting to the Cole-equation difficult or even erratic for the β-dispersion, because a substantial portion of the β-arc will be deluged by the much larger α-arc. At low frequencies (up to several kHz, α-range) the electrical impedance of intact skin is strongly influenced by the hydration of the stratum corneum [5,6]. At high radiofrequencies (above 200 MHz, γ-range) the water content of the tissue, not only of the stratum corneum, is measured as reflected in the dielectric constant [4,7]. Recent reviews on the physics and molecular biology of skin have been compiled by Forslind [8], and for oral mucosa by Squier and Hill [9].

For interpretation of impedance data it is important to understand what dispersions are involved and what they might reflect, and lack of this knowledge is probably the reason why the diagnostic power of electrical impedance has not yet been widely appreciated. For structural changes, the β-dispersion (from few kHz to several Mhz) should be the proper frequency range of choice [3,4].

METHODS

Our first study on oral mucosa involved measurement through the cheek. A small electrode on the area of investigation on the inside of the cheek and a large electrode on the outside concentrated the electrical test current in the mucous membrane, thereby reducing artefacts from the muscular layers and the skin, which were also included in the measured volume by this primitive technique [10]. A simple index reflecting extracellular oedema was formulated as the quotient between electrical impedance magnitudes measured at 20kHz and 1MHz, inspired by the literature on body composition analysis [11], where different pathways for electrical current of different frequencies are used to estimate e.g. intracellular and extracellular water. The principle is that low frequency currents are confined to the extracellular space, while high frequency currents can enter the interior of the cells by capacitive coupling through the cell membranes.

For the skin, a probe with fixed geometry was initially used with a manual impedance bridge, and the simple index was used for quantification of skin reactions. A fully automatic multifrequency impedance spectrometer, measuring magnitude and phase at 31 frequencies in the range 1kHz to 1MHz, was then developed. This automatic device was also facilitated with variable depth penetration by electronically varying the effective size of the electrode system [12]. Depth variation was first studied with the new automatic device using exposure to SLS, and the simple index [13].

In an attempt to extract more information from the impedance spectra, a set of four indices was introduced:

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\begin{align*}
MIX &= \text{abs}(Z_{20kHz})/\text{abs}(Z_{500kHz}) \\
PIX &= \text{arg}(Z_{20kHz})-\text{arg}(Z_{500kHz}) \\
RIX &= \text{Re}(Z_{20kHz})/\text{abs}(Z_{500kHz}) \\
IMIX &= \text{Im}(Z_{20kHz})/\text{abs}(Z_{500kHz})
\end{align*}
\]

where abs is the magnitude, arg the phase angle in degrees, Re and Im the real and imaginary parts of the impedance Z at the frequencies indicated [2,14]. The four indices have been used to differentiate various types of reactions to irritants and allergic agents (both delayed and immediate allergic reactions) [14-16]. Exposure to sodium lauryl sulphate, benzalkonium chloride, nonanoic acid, nickel sulphate, and common allergens used in prick tests were used. Recently a dedicated mouth probe has been developed, baseline data from various oral regions have been mapped [17], and irritative reactions have been studied [18].
RESULTS AND DISCUSSION

Early experiments revealed that electrical impedance already in its primitive implementation could detect irritative reactions in the oral mucosa with a magnitude below the visual threshold [10]. The same turned out to be true also for skin reactions induced by SLS, and was verified using the impedance spectrometer [19]. Different anatomical regions display typical baseline levels [17,20] for both skin and oral mucosa. Contra lateral or ipsilateral reference sites from the same region should preferably be used, or a test site could be followed in time before and after exposure to a test substance or other agent. If references cannot be made available, e.g. when the whole skin costume is affected, tolerance tables for various regions can be used, and have been provided by us [20]. The relative standard deviation increased with increasing depth setting [13]. It is thus possible to optimize depth setting for a certain reaction, depending on what skin (or mucous membrane) layers are involved.

In the frequency range 1 kHz to 1 MHz, the four indices seem to extract most of the information in the spectrum of intact skin or in skin with mild reactions [2,14]. This has also been demonstrated using a holographic neural network [21]. However, in strong reactions additional information can be extracted from the spectra by e.g. curve-fitting the Cole-equation to one dispersion at a time, because when the barrier function is severely damaged, the dispersions become enough separated. Patterns in the proposed indices seem to be powerful enough to discriminate between various types of conditions [2,14,15,21].

Electrical impedance is a powerful tool for quantification of skin reactions, or reactions in mucous membranes. It may also differentiate various conditions, difficult or impossible to separate by other means, by classification based on information in electrical impedance spectra.

REFERENCES