Quantification of Skin and Mucosal Reactions by Electrical Impedance

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Abstract: The electrical impedance of skin and mucous membranes is a highly sensitive indicator of induced irritative reactions, and can also reflect some allergic reactions and diseases. Until recently, the diagnostic power of electrical impedance has been considered rather poor. However, patterns of indices have now been suggested which apparently can discriminate some different types of reactions, and possibly discriminate irritative reactions from allergic ones. The simple indices used so far work well for weak reactions, as well as for strong reactions. For strong reactions, more information can be extracted using other indices or parameters. It is advised to use the proper sections of electrical impedance dispersions.

INTRODUCTION

It is known since the beginning of this century that structural and chemical changes in living tissue are reflected in electrical impedance changes. However, due to the complexity of biological materials, the connection between the behaviour of impedance parameters and physiological and pathological tissue conditions is generally difficult to establish. This is particularly true of skin, because information from several heterogeneous layers will be superimposed. Some general properties of a cellular structure were mapped by Cole already in the 30's [1], and the Cole-equation has been frequently used for extraction of Cole-parameters by curve-fitting. For relatively homogeneous tisssues such as muscle or blood, the Cole-parameters can be associated with structures such as cell membranes, and intracellular and extracellular volume conductors. Although the Cole-equation often provides an adequate fit to the measured data in a limited frequency range, it cannot be taken for granted that the Cole-equation is justified for heterogeneous structures such as intact skin, or intact mucous membranes [2].

Early investigators were limited in frequency range by available electronics, and some used only one frequency. The general behaviour of living tissue in a wide frequency range was mapped by Schwan [3], who defined the major dispersions. An excellent critical review has been compiled by Foster and Schwan [4]. For the interpretation of impedance changes it is obviously important to understand what dispersion is involved. For structural changes, the β-dispersion should be the proper choice. For intact skin and intact mucous membranes, the α- and β-dispersions are not well separated. The understanding of the physics and molecular biology of skin and mucous membranes is far from complete, partly because the necessary tools have only recently become available. Recent reviews on the subject have been compiled by Forslind [5] and Squier and Hill [6].

MATERIALS AND METHODS

The first study of ours 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 test current in the mucous membrane, thereby reducing artefacts from the muscular layers and the skin [7]. The mucosa was exposed to a variety of hard dental materials and some substances in liquid form. Originally the impedance was measured at 8 frequencies in the range 0.2Hz to 1MHz. Inspired by the literature on body composition analysis [8], an index reflecting extracellular edema was formulated as the quotient between the magnitudes at 20kHz and 1MHz.

For the skin, first a probe with fixed geometry was developed and used with a manual impedance bridge. Later, a fully automatic multifrequency impedance monitor, measuring magnitude and phase at 31 frequencies in the range 1kHz to 1MHz was developed. The automatic device is also facilitated with variable depth penetration by electronically varying the effective size of the electrode system [9]. First the ability to detect irritation below the visual threshold and variations between body regions were assessed, using the simple index and exposure to sodium lauryl sulphate (SLS) [10,11]. Then the method was compared with other bioengineering techniques [12]. The depth variation was studied using exposure to SLS, measurements with the automatic instrument and the simple index [13].

In an attempt to extract more information from the impedance spectra, a set of four indices was introduced and the possibility to differentiate different types of skin reactions was investigated, using exposure to SLS, benzalkonium chloride (BZ) and nonanoic acid (NON) [2,14]. The four impedance indices are:

$MIX=abs(Z_{20kHz})/abs(Z_{500kHz})$,

$PIX=arg(Z_{20kHz})-arg(Z_{500kHz})$,

$RIX=Re(Z_{20kHz})/abs(Z_{500kHz})$ and

$IMIX=Im(Z_{20kHz})/abs(Z_{500kHz})$, 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. Allergic contact skin reactions have also been studied, using exposure to nickel sulphate and the simple index [15], and compared with irritative reactions using the set of four indices [16].

Recently a dedicated mouth probe has been developed, and baseline data from various oral regions have been mapped.

RESULTS AND CONCLUSIONS

Early mucosal tests revealed that the method already in its primitive implementation could detect irritant reactions with a magnitude below the visual threshold [7]. The same held for skin reactions induced by SLS [10].

There are differences in baseline level for different anatomical regions of skin [11]. The same holds for different oral regions (unpublished data). Thus, contra lateral or ipsi lateral reference sites from the same region should be used, or a test site could be followed in time before and after exposure to a test substance or other agent. References should always be used, because individual variations are far from negligible.

Electrical impedance, using the simple original index, was at least as sensitive as transepidermal water loss, and more sensitive than visual scoring, laser Doppler flowmetry and Corneometer readings (estimating water content by electrical capacitance) [12] for detection of irritant skin reactions.

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 layers are involved. If different types of reactions should be compared under the same conditions, it is recommended that maximum depth is used, because data measured in this mode will contain information from all layers penetrated by the test current.

The four indices seem to extract most of the information in the spectra of intact skin, or in skin with mild reactions [2,14]. However, in strong reactions more information can be extracted from the spectra, using more indices from other sections of the spectra [2], or by curve fitting to some model [17]. E.g. the Cole-equation could be applied to one dispersion at at 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 reactions [2,14,16]. Other objective investigative methods, such as skin biopsies, molecular biology or biochemistry should be combined with electrical impedance to verify the connection between structural and functional properties and the behaviour of electrical impedance patterns.

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