Dissertations

Skin Sensitivity Testing - A Biophysical Approach

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Miruna Nyrén *(middle)* defended her thesis on 3 May 2002 at the Department of Dermatology, Huddinge University Hospital. The External Examiner was Gregor Jemec *(middle right)*, Department of Dermatology, Roskilde University Hospital, and the Chairman of the reviewing board was Lennart Emtestam *(middle left)*. Peter Lidbrink *(right)*, Head of the department, and Stig Ollmar *(left)*.

The medical history and clinical examination are the main tools used to study dermatological diseases. The skin is the most readily accessible organ and visual inspection is easily done, but the disadvantage of this method is that it is subjective which makes it difficult to use as a research tool because it is open to bias. Furthermore, visible skin lesions are already per se at an advanced stage of their evolution since signs that are detectable with the naked eye are always preceded by histological and/ or biochemical changes. Various bioengineering techniques have been proposed for assessing skin properties. Objective and non-invasive methods are needed to assess skin reactions in clinical work and research. Many devices for non-invasive evaluation of the skin are available. These methods include measurements of a) transepidermal water loss, b) the moisture content of the stratum corneum using electrical capacitance or conductance, c) cutaneous blood flow using laser Doppler flowmetry, d) skin colour, and e) the acoustical properties of the skin using ultrasound.

In our studies, we have compared a new bioengineering technique, based on electrical impedance, with more established methods, such as transepidermal water loss (TEWL), electric capacitance moist measurements (EMC), laser Doppler flowmetry (LDF) and visual evaluation.

Bioimpedance can be measured if electricity from an external source is applied to the living organism being studied. Such measurements give information about electrochemical processes in the tissue and can be used to characterise the tissue or monitor pathophysiological changes. Bioimpedance is frequency-dependent and differs greatly among various cell suspensions and tissues, and significant changes in electrical properties are also found when cells or tissues change from one physiological state to another, e.g. living to dead, dry to moist or normal to pathological. In living organisms, electrical conduction is related to the water and electrolyte distribution in the biological conductor. The living organism contains intra- and extra-cellular fluids, which behave as electrical conductors, and cell membranes that act as imperfect reactive elements. At low frequencies (1kHz), the current passes mainly through extra-cellular fluids but at higher frequencies (500–800 kHz), it penetrates both intra- and extra-cellular fluids. Thus, body fluids and electrolytes are responsible for electrical conductance (e.g. 1/ resistance) and cell membranes are involved in capacitance. In biological structures, application of a constant, low alternating current produces a potential due to the impedance of the tissue below the probe, which is frequency-dependent. Technology based on electrical impedance has been used for medical purposes since the early 1920s, but it was not until the past few years that new instruments and methods become available for various clinical applications, e.g. cardiopulmonary tomography, skin hydration, detection of dental decay, or cervical neoplasia and skin pathology.

The more specific aim of this thesis was to evaluate the electrical impedance device for detecting skin irritation (I), distinguishing between irritant and allergic contact skin reactions (III), studying tuberculin reactions (IV) and measuring reactions to the prick test (V). The baseline values of the electrical impedance at various anatomical sites of the skin and their relation to age and gender were also studied (II).

In paper I, we used a new, non-invasive impedance device together with three other bioengineering techniques (TEWL, EMC, LDF), besides visual scoring, to monitor the degree of damage and the healing process of skin irritation induced by SLS in 10 healthy subjects. A simple impedance index was obtained, also called the electrical impedance index (IX), based on manual measurements using a provisional laboratory set-up. Our results suggest that electrical impedance is well suited as an objective tool for measuring the response of the skin to irritation. This method seems at least as sensitive as other bioengineering techniques. In paper II, baseline electrical properties of the skin were studied at 10 different sites in 131 healthy volunteers. We found significant changes in the impedance parameters related to age, but to a lesser extent between men and women. Since the electrical impedance of the skin varies significantly between different skin regions, the sites for controls and the actual test site must be very carefully selected. Baseline values are also useful in studies where contra or ipsilateral controls are not available. In paper III, we studied irritant and allergic contact reactions of 33 nickel-allergic patients with TEWL and electrical impedance measurements. The changes in impedance indices of the reactions had a distinctive pattern. The data suggest that the method used to measure electrical impedance is of value for distinguishing between contact reactions of allergic and irritant nature. In paper IV, we studied tuberculin and SLS reactions of 20 healthy volunteers known to be PPD-sensitive. Unlike the irritant reactions, the degree of inflammation in the dermal infiltration induced by the tuberculin test could not be detected by changes in TEWL, probably because the epidermal skin barrier is completely intact. The electrical impedance response pattern of the tuberculin reaction differs from that of the SLS contact reaction. These findings clearly indicate that electrical impedance is useful, not only for studies of contact dermatitis, but also of the tuberculin reaction. In paper V, wheals were induced in 10 allergic patients by performing skin prick tests with the relevant allergen and histamine. The wheals were evaluated using laser Doppler and electrical impedance. Our findings suggest that the wheal reaction can be characterised objectively and quantified using the electrical impedance technique.

The main conclusion of this thesis is that, compared to visual scoring, additional information about experimentally induced skin reactions is obtained with non-invasive bioengineering techniques, especially when several methods are used together. It is tempting to speculate that non-invasive bioengineering techniques, including a newly developed impedance instrument, could be of value in the clinical management of inflammatory skin diseases.

The thesis is based upon the following original papers.

I. Ollmar S, Nyrén M, Nicander I, Emtestam L. Electrical impedance compared with other non-invasive bioengineering techniques and visual scoring for detection of irritation in human skin. Br J Dermatol 1994; 130: 29–36.

II. Nicander I, Nyrén M, Emtestam L, Ollmar S. Baseline electrical impedance measurements at various skin sites - related to age and sex. Skin Res Technol 1997; 3: 252–258.

III. Nyrén M, Kuzmina N, Emtestam L. Electrical impedance as a potential tool to distinguish between allergic and irritant contact dermatitis. In press. J Am Acad Dermatol.

IV. Nyrén M, Hagströmer L, Emtestam L. Instrumental measurement of the Mantoux test: differential effects of tuberculin and sodium lauryl sulphate on impedance response pattern in human skin. Dermatology 2000; 201: 212–217.

V. Nyrén M, Ollmar S, Nicander I, Emtestam L. Electrical impedance assessment of wheals. Allergy 1996; 51: 923–926.