

Short communication

An electrical impedance technique for assessment of wheals

Nyrén M, Ollmar S, Nicander I, Emtestam L. An electrical impedance technique for assessment of wheals.

Allergy 1996; 51: 923–926. © Munksgaard 1996.

In previous studies of the electrical impedance of the skin, we introduced a set of physical indices which could be used to distinguish between the cutaneous effects produced by different irritants and allergic contact reactions. In this study, wheals were induced in 10 allergic patients by performing prick tests on the forearm with the relevant allergen and histamine, respectively. Normal skin was used for control. The wheals were evaluated by visual scoring, laser Doppler, and electrical impedance. As expected, there was a close agreement between the visual and laser Doppler readings. Compared to the controls, there were significant changes in the electrical impedance of the wheals, especially in the index related to the phase angle. The changes in the indices were found to follow a particular pattern, which diverged from those obtained in contact skin reactions of both allergic and irritant type. Our results indicate that, by the application of the impedance technique, it will be possible to characterize objectively and quantify the wheal reaction. The results also suggest that cutaneous reactions of completely different causes, such as allergic skin reactions of the late and immediate type, and irritant contact reactions, may be distinguished on the basis of their effects on the electrical impedance of the skin.

**M. Nyrén¹, S. Ollmar², I. Nicander^{1,2},
L. Emtestam¹**

¹Department of Dermatology, Huddinge University Hospital, S-14186 Huddinge; ²Center for Oral Biology, Karolinska Institute, Huddinge, Sweden

Key words: allergy; electrical impedance; hives; laser Doppler.

Miruna Nyrén, MD
Department of Dermatology
Huddinge University Hospital
S-141 86 Huddinge
Sweden

Accepted for publication 30 May 1996

In the clinic, visual inspection and measurement of size are the normal way of evaluating wheals, and the results show some variability depending on the observer (1). More objective methods of assessment have been used such as ultrasound and laser Doppler flowmetry (LDF) (2–4). We have recently described a noninvasive method based on electrical impedance which seems to be a suitable tool for skin investigations (5–7).

This study aimed to evaluate the electrical impedance technique for the investigation of immediate skin reactions induced by common inhalant allergens, and to see whether the patterns of the impedance indices differ from the ones obtained in our studies on contact reactions.

in the study. All of them had a history of hay fever or mild bronchial asthma and were selected on the basis of a previous positive prick test on a standard panel of inhalant allergens at the Department of Dermatology, Huddinge University Hospital, measured according to the EAACI recommendation (8). All antihistamine medication was discontinued 1 week before the test. None of the test subjects used theophylline or p.o. steroid medication. One of the test subjects inhaled β_2 -agonists on a regular basis. Informed consent was obtained from all participants, and the study was approved by the local ethics committee. The measurements were performed from April to September 1995.

Material and methods

Test subjects

Ten white volunteers, six women and four men, aged 18–43 years (mean 34 years), participated

Test substances

Skin prick tests were performed with the following four common inhalant allergens: birch, timothy, cat, and mite with SoluprickTM (10 HEP, Allergologisk Laboratorium ALK, Hørsholm, Denmark). The

positive control liquid was 10 mg/ml histamine dihydrochloride (ALK).

Test procedure

A volume of 40 µl of relevant allergen extract was placed on the skin on the midvolar aspect of the forearm, and 40 µl histamine solution on the opposite side. A superficial prick was made through the test solution with Microlance™ (Becton Dickinson, USA). The test substances were applied randomly on the left or right arm. The test sites were marked with ink. An immediate wheal-and-flare reaction was detected and recorded after 15 min (visual scoring). The skin test sites were quantitatively assessed at the center of the wheals by the impedance technique and LDF. After application of the allergen, readings were taken every 15 min for 2 h in the following order: 1) visual assessment, 2) LDF, and 3) electrical impedance. Impedance was used last, because the surface of the skin had to be soaked with physiologic saline solution in order to short-circuit the naturally high impedance of the stratum corneum before application of the impedance probe.

Evaluation methods

Visual assessment. The wheal size was used to quantify the skin reaction by comparing the allergen wheal to that of histamine by the system described by Aas & Belin (1).

Laser Doppler flowmetry (LDF). LDF was performed with Periflux™ Pf2 (Perimed AB, Stockholm, Sweden) (9, 10). The LDF probe was mounted in a rubber block 5×5×1 cm to ensure stable positioning on the skin. The mean of two LDF measurements from each test site was used.

Electrical impedance. Electrical impedance was measured with a SCIM™ skin electrical impedance spectrometer (SCIM Medical AB, Kinna, Sweden), as previously described (6, 11). In short, this instrument records magnitude and phase spectra of impedance at 31 logarithmically distributed frequencies in a defined volume under the probe. This volume can be selected to include contributions, stepwise, at five different skin depths. The four indices used, representing changes with frequency along the four major aspects of electrical impedance space (11), are as follows:

- Magnitude index, MIX=abs(Z_{20 kHz})/abs(Z_{500 kHz})
- Phase index, PIX=arg(Z_{20 kHz}) – arg(Z_{500 kHz})
- Real part index, RIX=Re(Z_{20 kHz})/abs(Z_{500 kHz})

Imaginary part index, IMIX=Im(Z_{20 kHz})/abs(Z_{500 kHz}) where abs(Z_i) is the magnitude (modulus) of the complex electrical impedance at the frequency *i*, arg(Z_i) the argument (phase angle) in degrees, Re(Z_i) the real part, and Im(Z_i) the imaginary part of the complex electrical impedance.

Statistics

The Wilcoxon signed rank test was used to compare results expressed as means before and after exposure. A *P* value ≤0.05 was considered significant.

Results

A total of 10 patients were included in the study; seven were tested with birch pollen, one with cat allergen, one with timothy allergen, and one with mite allergen. The 2-h readings were performed in nine patients only.

Visual scoring

The wheal elicited by histamine was at least 7 mm in diameter for all patients after 15 min. The wheal elicited by allergen was scored as follows: four test subjects were 4+, five were 3+, and one was 2+ after 15 min.

Laser Doppler

Both the formation of the wheals and the recovery were clearly detected by the LDF. In all patients, compared to the controls, 15 min after the prick test, there were statistically significant changes of the means for histamine sites as well as for allergen sites (*P*≤0.01) (Table 1). After 1.5 h, the mean value for histamine had returned to the range of pre-exposure values. For allergen, in contrast, the mean values had not returned to the basal level range after 2 h (Fig. 1).

Table 1. Means of measurements of test sites exposed to histamine or allergen compared with controls by LDF and electrical impedance at 15 and 30 min and 2 h by Wilcoxon signed rank test. Level of significance is shown

		Histamine 15 min	Allergen 15 min	Histamine 30 min	Allergen 30 min	Histamine 2 h	Allergen 2 h
IMP	MIX	0.01	NS	NS	0.01	NS	NS
	PIX	0.01	0.01	0.01	0.01	0.01	NS
	RIX	NS	NS	0.05	NS	NS	NS
	IMIX	NS	NS	NS	0.05	NS	NS
LD		0.01	0.01	0.01	0.01	NS	0.01

NS: not significant.

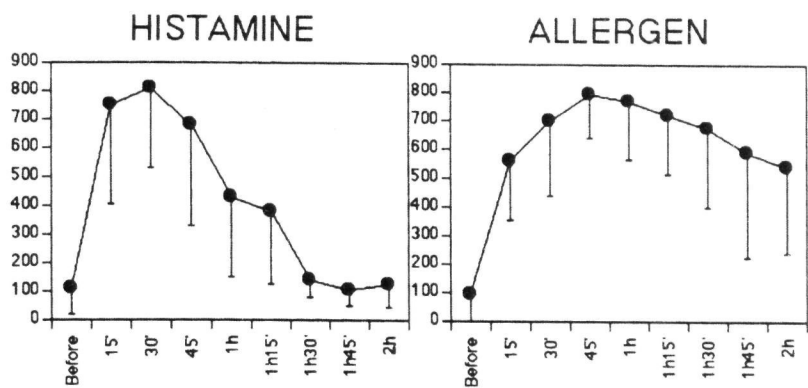


Fig. 1. Mean values and standard deviation for measurements of test site with laser Doppler flowmetry before and after application of histamine and allergen. Measurements were taken every 15 min for 2 h.

Electrical impedance

The mean values and the standard deviation were calculated for the four indices at all test sites. Data from depth settings 1 and 5 were analyzed, and only depth 5 is presented. Depth 5 includes information from all the more superficial depth settings. The pathophysiologic events in a prick test are mainly located in the dermis, i.e., at a depth requiring depth setting 5 to obtain maximum signal. Results for the four indices are given in Fig. 2. Table 1 summarizes the statistical analysis for depth setting 5.

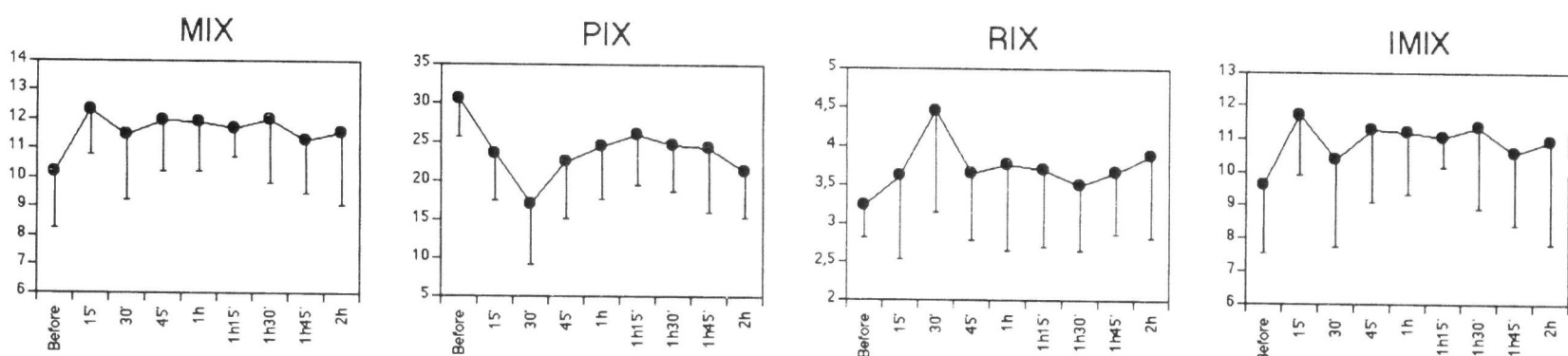
Discussion

The main goal of this study on wheals was to compare the technique based on electrical impedance with the two established methods of visual scoring and LDF. Several visual scoring systems of wheals that work well exist in the clinic, but the subjective factor introduces interobserver variability (8). LDF has been used extensively by many workers to measure blood flow of various situations, and has also been applied to measure wheals. In the study by Serup & Staberg (3), LDF showed good agreement with visual assessment of wheals, but they stated that intra- and interindividual variations in skin blood flow were significant.

In the study reported here, we have used a new, noninvasive impedance device which, in contrast to previous impedance methods (12, 13), enables measurements to five different depths (6, 11). The wheal response reflects changes in the electrical properties of the skin and is correlated to changes of the electrical impedance indices (Fig. 2).

Another important result of this investigation was in the response pattern of the four indices. In previous studies, where contact reactions, allergic as well as irritant, were induced in patch tests, the indices also expressed statistically significant changes, but in other ways (11, 14). In MIX, the

HISTAMINE



ALLERGEN

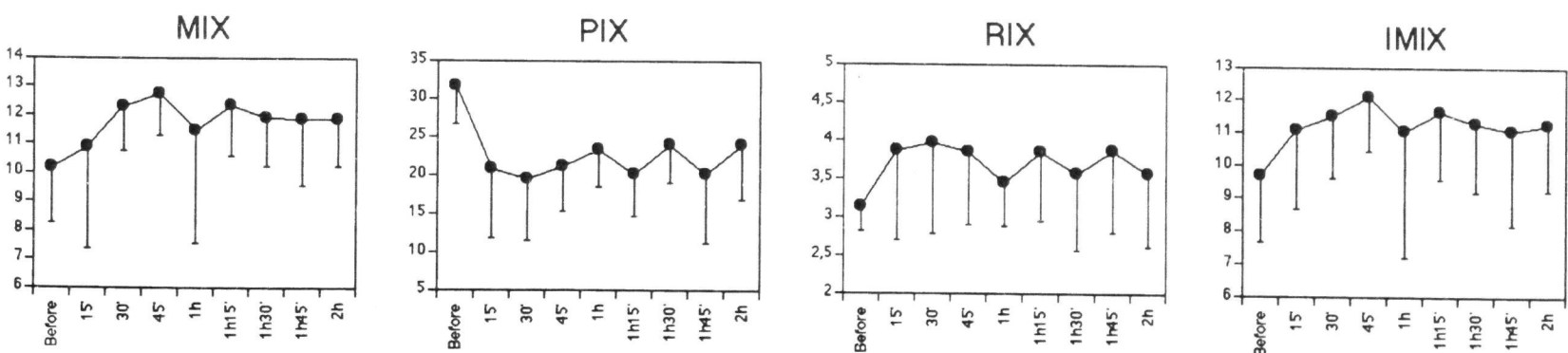


Fig. 2. Mean values and standard deviations for skin responses as reflected in four electrical impedance indices MIX, PIX, RIX, and IMIX at each observation time before and after prick testing with histamine and allergen, respectively, during 2 h for depth setting 5.

change in allergic contact reactions is due mainly to alterations at higher frequencies, whereas in irritant reactions changes are largely due to alterations at lower frequencies (11). In this study of wheals, the largest changes were of the phase angle of the electrical impedance, giving a decrease of the index PIX, and this finding was statistically significant for both test sites on wheals induced by histamine and those induced by inhalant allergens at 15 and 30 min with depth setting 5. Although the laser Doppler signal is stronger, this method can only quantify the response. The impedance signal is strong enough for quantification, and the impedance method further aids the ability of classification by index patterns.

In conclusion, electrical impedance in its newly presented form, with local measurement to a selected depth, seems suitable for the detection of wheals induced by histamine as well as common inhalant allergens by prick tests. By implementation of this electrical impedance method, in clinical and experimental situations, it should be possible to distinguish skin reactions of different types.

Acknowledgments

We thank Dr Reidar Grönneberg for critically reading the manuscript. This study was supported by grants from the Swedish Council for Work Life Research (95-0266), the Swedish Society of Medicine, the Swedish Society of Medical Research, the Edvard Welander Foundation, the Finsen Foundation, and the Tore Nilson Foundation.

References

1. Aas K, Belin L. Suggestion for biologic qualitative testing and standardization of allergen extracts. *Acta Allergol* 1974;29:238-40.
2. Serup J. Diameters, thickness, area, and volume of skin-prick histamine weals. Measurement of skin thickness by 15 MHz A-mode ultrasound. *Allergy* 1984;39:359-64.
3. Serup J, Staberg B. Quantification of weal reactions with laser Doppler flowmetry. *Allergy* 1985;40:233-7.
4. Staberg B, Serup J. Allergic and irritant skin reactions evaluated by laser Doppler flowmetry. *Contact Dermatitis* 1988;18:40-5.
5. Emtestam L, Ollmar S. Electrical impedance index in human skin: measurements after occlusion, in 5 anatomical regions and in mild irritant contact dermatitis. *Contact Dermatitis* 1993;28:104-8.
6. Nicander I, Ollmar S, Lundh Rozell B, Eek A, Emtestam L. Electrical impedance measured to five skin depths in mild irritant dermatitis induced by sodium lauryl sulphate. *Br J Dermatol* 1995;132:718-24.
7. 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;30:29-36.
8. Dreborg S, Backman A, Basomba A, Bousquet J, Malling D. Skin tests used in type I allergy testing. EAACI position paper. Subcommittee on Skin Tests. *Allergy* 1989;44 Suppl 10:15.
9. Frödin T. Evaluation of the state of the skin by assessing cutaneous barrier function, blood flow and water content. Thesis, 1988, University of Linköping, Sweden.
10. Nilsson GE, Tenland T, Öberg PA. Evaluation of a laser Doppler flowmeter for measurement of tissue blood flow. *IEEE Trans Biomed Eng* 1980;27:597-604.
11. Nicander I, Ollmar S, Eek A, Lundh Rozell B, Emtestam L. Correlation of impedance response patterns to histological findings in irritant skin reactions induced by various surfactants. *Br J Dermatol* 1996;134:221-8.
12. Salter DC. Quantifying skin disease and healing *in vivo* using electrical impedance measurements. In: Rolfe P, editor. *Non-invasive physiological measurements*. London: Medical Physics Series, 1979:21-64.
13. Yamamoto T, Yamamoto M. Analysis for the change of skin impedance. *Med Biol Eng Comp* 1977;15:219-27.
14. Nicander I, Ollmar S, Lundh Rozell B, Emtestam L. Mild allergic contact reactions in the skin assessed using electrical impedance (submitted).

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.