EVALUATION OF PATCH TESTS RESULTS – RESEARCH AND DEVELOPMENT OF TECHNIQUE BASED ON INFRARED THERMOGRAPHY

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Summary

Skin tests in allergology are a method of medical diagnosis that attempts to provoke a small, controlled allergic response. Evaluation of the patch test depends on visual assessment so it is not an objective method, because it does concern only skin surface and difficulties like changes in skin pigmentation, atopic skin, black race skin or delayed reaction may occur. Studies with use of thermography confirm that skin surface allergic reaction is strictly connected with temperature increasing at that area so such technique may be the key for impartial evaluation. Carried out tests, also confirmed information from literature review, that to obtain valuable infrared images large intervals between allergens must be kept.

Keywords: medical thermography, allergology, image analysis

OCENA WYNIKÓW TESTÓW PŁATKOWYCH – BADANIE I ROZWIJANIE
METODY OPARTEJ NA TERMOGRAFII

Streszczenie

Testy skórne w alergologii to metoda diagnostyczna polegająca na wywołaniu małej, kontrolowanej reakcji alergicznej. Ocena testów płatkowych oparta jest na ocenie wizualnej, której podlega tylko powierzchni skóry, a więc nie jest obiektywna, gdyż mogą mieć na nią wpływ takie czynniki jak zmiany w pigmentacji skóry, skóra atopowa, skóra rasy czarnej lub opóźniona reakcja. Badania z użyciem termografii potwierdziły, że reakcja alergiczna powierzchni skóry jest ściśle powiązana ze wzrostem temperatury w tym obszarze, więc technika ta może być kluczowa w dążeniu do obiektywnej oceny. Przeprowadzone badania potwierdziły także informację z przeglądu literatury, że aby otrzymać wartościowe termogramy należy zachować duże odstępy pomiędzy aplikowanymi alergenami.

Słowa kluczowe: termografia medyczna, alergologia, analiza obrazów

1. INTRODUCTION

Dermatological diagnostic of dermatitis and allergy diagnostics in many cases is still based on subjective techniques of evaluation. In allergology the clinical evaluation of skin test reaction is achieved by visual impression combined with measurements of the intensity of the reaction on the usual scale of differentiation. In this paper authors presents results of carried out tests with the use of infrared thermography which were undertake to check out if it can improve assessment of commonly used non-objective techniques of evaluating patch tests and conception of dedicated measurement stand developed for further standardization of reading procedure.

Thermography is a valuable, non-contact measurement technique, which can find practical application in dermatological diagnostics, but only if all standardisation rules are adhered, appropriate terms and conditions in consulting room and patient's preparation among other things. Every negligence in testing procedure may produce an effect that may distort a result, and make it useless. It can be useful not only in diagnosis of skin tumours, particularly melanoma, or burn diagnostics, but also in allergy diagnosis, which is more and more common disease.

According to [1][2][3] the essence of the thermography is to compare temperature of skin with positive reaction to allergen with temperature of surrounding healthy skin, so information about gradient of temperature is more important than its

absolute value. Maximal gradient for the strongest allergic reactions is within 2 and 3°C (accuracy of measurement depends on parameters of used camera).

Skin tests are commonly used in allergic diagnostics. It is a method of medical diagnosis that attempts to provoke a small, controlled, allergic response. In patch test, which are used for diagnostics of allergic contact dermatitis, strips of tape containing small quantities of common allergens are applied onto the skin, usually on the back, for forty eight hours incubation. The skin reaction is observed at regular intervals, usually after 2, 3 and 4 days. Evaluation of the test depends only on visual assessment. It is not an objective method, because it does concern only skin surface and difficulties like changes in skin pigmentation, atopic skin, black race skin or delayed reaction may occur. Additional reading after 7 days might disclose another positive reactions for allergens which were negative in previous readings. [4][5]

Patch test diagnostics reduces costs of treatment and improves quality of life because it enables and shorten final diagnosis. Results of such tests help to avoid identified allergic haptens, thus help reduce symptoms, so it is important to do not omit delayed reactions. [4][5]

Allergic reactions occur when a person's immune system reacts to normally harmless substances in the environment (allergens). This reaction results in an inflammatory response with release of proinflammatory cytokines increase permeability of blood vessels and with typical local symptoms like redness, increase temperature and oedema. Studies with use of thermography confirm that skin surface allergic reaction is strictly connected with temperature increasing in that area. Carried out tests also confirmed information from the literature review, that large intervals, like 8 to 10 cm, between allergens must be kept. [1][2]

Recently there is more and more publications about thermography as an additional technique for patch tests to increase the index of properly diagnosed allergic reactions. For example in cases described in [2] the evaluation of patch test was performed 30 minutes after patch removal. Positive reactions to allergen varied from "+" to "++++" (according to criteria of the International Contact Dermatitis Research Group), and in thermograph was shown as hot area which extended beyond the visible borders of the patch site and was asymmetrically oriented towards the nearest lymph node, spreading as one or more hyperthermic lines. That is the reason to keep large intervals between patches, like 8 to 10 cm. It was also established that temperature and quantity of applied allergens have influence on the temperature of tested skin surface, so solutions should be heated up to the ambient temperature (about 20-23°C) and applied in small quantities.

2. DIAGNOSTIC METHOD AND STANDARDISATION

Patch testing is the only useful and reliable method for identification of an allergic contact dermatitis – it is acknowledged as the gold standard. For over forty years major role in the standardisation of patch testing had the International Contact Dermatitis Research Group (ICDRG) which was formed to promote the understanding of contact dermatitis. [5]

Infrared thermography appeared as an diagnostic technique in medicine at the early 1960s and first publications on standardisation of thermal imaging were published in the 1970s. Few years ago the International Standard Organization has published two new standards to define the use of a thermography in fever screening. The first one, IEC 80601-2-59:2008, describes particular requirements for the basic safety and essential performance of screening thermography for human febrile temperature screening, and the second one, ISO/TR 13154:2009, defines deployment, implementation and operational guidelines for identifying febrile humans using a screening thermograph. However it is about fever screening it provides some guidelines for application of thermal imaging in clinical medicine. These documents dictate standards in manufacture and performance and are specific in the description of calibration procedures. [4][7][9][10]

Emissivity of biological tissues is within 0.85 and 0.98. For human skin it is reported to be equal 0.98 ± 0.01 for wavelength range of 2-20 µm, it peaks around 10 µm, regardless of skin colour. Generally, for medical applications narrower wavelength band is used, from 8 to 12 µm. [1]

2.1. Patch test – procedure, evaluation and diagnosis

Patch testing is performed as follows: strips of tape containing small quantities of common allergens are applied onto the skin, usually on the back or on the arm, and it must remain in place and be kept dry for 48 hours. At this time the surface of application should not be rubbed by, for example, an underwear or be scratched in case of false positive reactions. The patient should not take any cortisone medication during the test and avoid exposure of the back to the sun. After that time patches are removed and after several minutes initial reading is performed. After another 1 or 2 days final reading is made. At

Fig. **1** the procedure of applying patch tests is presented.

Evaluation of test results is based on visual scheme. It is proceeded by physician on the basis of visual observation. Positive reaction at initial reading is classified as irritant contact dermatitis,

while at further readings positive reaction is classified as allergic contact dermatitis (ACT).
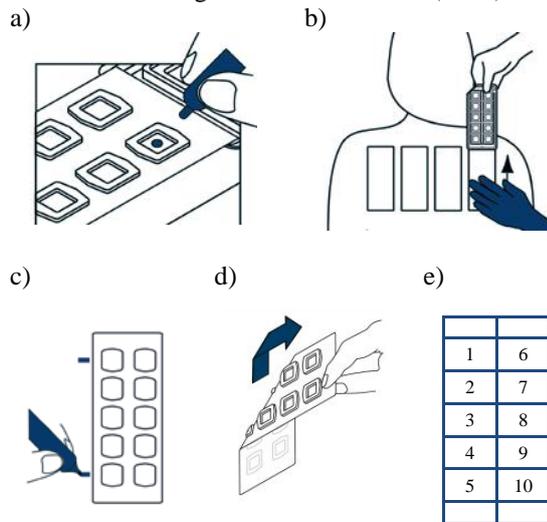
a)   b)

c)   d)   e)

Fig. 1. Applying patch test procedure: a) applying the test preparations, b) applying the unit of chambers onto the back, c) marking chambers, d) removing the patches after 48 hours, e) Arrangement of allergens on the back for strip with 10 chambers [12]

2.2. Standardisation

IR camera should be mounted perpendicularly to the examined surface, emissivity should be settled at 0,98 and sensitivity and accuracy should be defined.[1] Consulting room has to fulfil the following requirements: ambient temperature within 20-23°C, air humidity within 45-55%, lack of external heat and radiation sources, no draught and right space. Those parameters have to be written down in the test record form.

In case of thermal imaging important part of examination is patient's preparation. It is not allowed to apply substances, medications or drugs and to practise physical exercises even for a few days before test application. Before readings patient should come calmly and for 15 to 30 minutes stay in rest at waiting room. Then acclimatization in consulting room with undressed parts of the body, which will be studied, takes from 5 to 30 minutes. Such rules have to provide better accuracy and repeatability of the measurements. [6][7][8]

Tab. 1. Descriptive interpretation scale [5]

Grade	Meaning / appearance
-	Negative reaction
R	Irritant reaction
+/- or ?	Doubtful reaction
+	Light erythema, non-vesicular
++	Edema, erythema, discrete vesicles
+++	Coalescing vesiculobullous papules

Fig. 2. A visual scheme for the interpretation of the test result [12]

The International Contact Dermatitis Research Group for interpretation of patch test results recommends to use descriptive interpretation scale. Example of such scale is presented at Tab. 1 and its visual scheme at Fig. 2.

Common problem occurring during patch test results evaluation is connected with interpretation of lesions as irritant, doubtful and weak reaction, especially at second reading, when uncertain grades are not allowed. In practice the difference between doubtful and weak reaction at initial reading is that if it is a weak reaction and it is negative at second reading it is an irritant allergen and then the prevention is to avoid contact to reduce symptoms like rash and red skin, and if reaction is doubtful and at another reading it is negative then patient is not allergic to that allergen. The issue is that in case of negative grade at second reading it matters if interpretation of reaction at first reading was either doubtful (+/-) or weak (+). Wrong diagnostics extends time of final diagnosis, generates costs by necessity of another physical and causes discomfort of a patient.

3. DIAGNOSING WITH THE USE OF THERMOGRAPHY TECHNIQUE

In this chapter the measurement procedure is presented. It will be used for further improvement of objective identification of dermatitis in patch tests. The procedure of measurement for initial reading is shown on the diagram at Fig. 3. Proceedings in second and third (if was performed) reading is without strips removal.
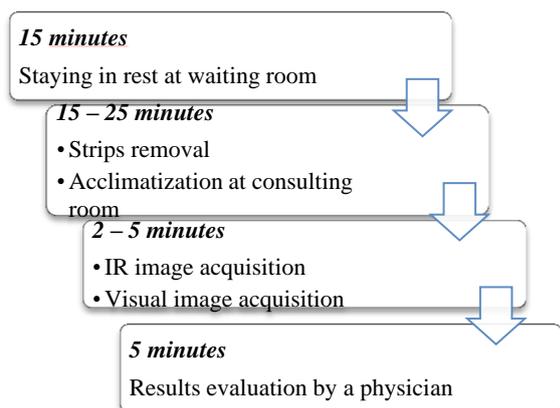
Fig. 3. Diagram of measurement procedure of initial reading after 48 hours

Patients were examined within proposed measurement procedure at the Medical Centre Med-All in Krakow, during standard patch tests. Reading were performed after two and four days after application. In some cases additional reading was held after 7 days.

Tests were proceeded on group of 48 patients (23 females, 8 males, aged 16-69 years and 17 children under 16 years). Among this group only 3 individuals had earlier diagnosed allergic contact dermatitis. All participants provided written informed consent. The study was performed for 16 months between 2013 and 2014.

3.1. Terms and conditions at consulting room

Measurements were carried out in a consulting room with ambient temperature within 20-21°C, air humidity within 50-55%, lack of external heat and radiation sources, no draught and right space. Distance between camera and subject was equal about 1 m, because then atmospheric influence can be neglected and this distance was appropriate for chosen infrared cameras. IR camera were positioned perpendicularly to the examined surface, emissivity were settled at 0,98 and temperature scale were fixed to the patient.

3.2. Preparation of a patient

Patients were instructed that strips have to stay dry and that it is not allowed to scratch at application surface, take any cortisone medication and exposure of the back to the sun. To get valuable thermographic data the temperature of examined skin had to be stabilized before readings. That is why patients were performed acclimatization procedure, which was as follows: come calmly to the medical centre, at waiting room stay in rest for 15 minutes, in case of first reading after strips removal wait about 15-25 minutes with parts of the body which were irritated undressed, after initial reading do not scratch, wash or apply any ointment to one's surface of test application on the skin until next

reading, unless doctor decides otherwise. In case of another readings, procedure is the same with the exception of the fact that strips were removed previously.

4. MEDICAL EXAMINATION

At figures below patch test results of three representative cases are presented.

The first patient (Fig. 4, Fig. 5) with earlier diagnosed allergic contact dermatitis to applied allergen had single chamber on the arm. Visual evaluation of physician at initial reading was negative reaction (-), and at second reading – extreme reaction (+++), while at thermograph positive result is well visible at both readings. It is superb visible example of delayed reaction. In this case visual symptoms were visible after 4 days, but it might last longer.

Fig. 4. Example of delayed reaction. Visual grade: negative reaction after 2 days (left) and extreme reaction after 4 days (right)
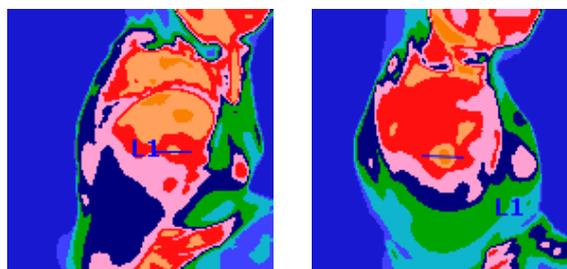

Fig. 5. Example of delayed reaction. Thermograph after: 2 days (left) and 4 days (right)

Another patient (Fig. 6, Fig. 7) had extreme reaction at two allergens. Physican graded allergens with number 9 and 10 as +++ at first reading, and the same at another reading (Fig. 6). At thermograph evaluation was more difficult because thermal reaction of the skin was so huge that it covered almost half of skin surface which was incubated (Fig. 7). There is no doubts that the patient is allergic to those two allergens but there is no certainty that he is not allergic to allergens from neighbour chambers.
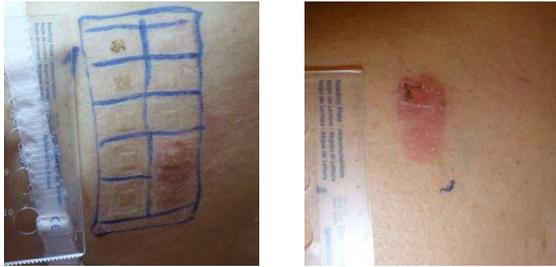
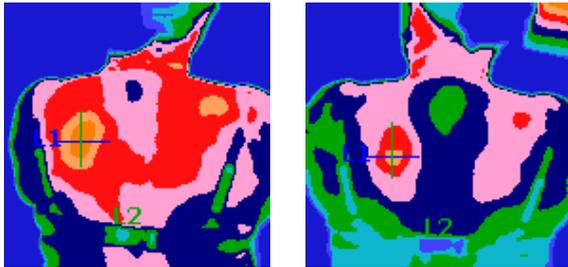Fig. 6. Example of extreme reaction after: 2 days
(left) and 4 days (right)

Fig. 7. Example of extreme reaction. Thermograph
after: 2 days (left) and 4 days (right)

In medical diagnosis it is necessary to strictly define lesions, as it is shown at Tab. 1 (chapter 2.2). When evaluation is performed with the use of thermographic techniques, identification of lesions is made on the basis of local thermal field disturbance and, what is important, in some cases it is impossible to define dermatitis only on the basis of thermograph. In such cases, for further research, it is planned to use multimodal image processing technique, which effects in synergy between observation and analysis of infrared data and vision data. It enables to introduce another stage to improve objectivity of dermatitis assessment.

5. CONCEPTION OF DEDICATED MEASUREMENT STAND

What follows from this research will be used to build dedicated measurement stand and for further standardization of reading procedure. The main aim of designing such stand is to reach better results with slighter feeling of discomfort during medical examination.

Developed prototype system for patch tests evaluation consist of four main components:
- Infrared camera
- Industrial camera
- Peltier's module
- Mobile computer for image acquisition and control of infrared camera.

The main part of measurement stand is a box mounted on a tripod stand. It contains both cameras and additionally, for better visualisation, 3D scanner is used. Application of this two types of cameras will enable its correlation. After geometrical calibration obtained images will be overlapped for more precise analysis.
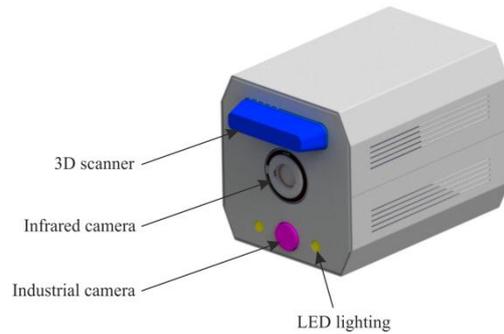

Fig. 8. Developed measurement box

Peltier module is used as a reference temperature for temperature reading. It gives opportunity to compare images from different readings of the same patient as well as different patients. It has been designed in close cooperation with measurement box on the folding arm.

Merit of this stand is that it is not bulky, the measurement is made at distance between 0,4 to 1 m from the patient and it does not have any special requirement to operate, so it is possible to use it even in a small consulting room which meets the criteria listed at chapter 2.2.

Image acquisition is accomplished with the use of ThermoAnalysis software, MONIT SHM. It also enables advanced image processing and analysis to extract diagnostic features of infrared images. Medical diagnostics is controlled and grouped in the projects with the possibility to create IR processing timestamp which allows to create different sections with subsequent processing techniques and parameters, thus provide to plan many diagnostic scenarios for acquired IR data and lead to compare various processing algorithms.

6. CONCLUSIONS

Main conclusion from carried out tests is that described method is effective and when standards are adhered it gives valuable results. It is important to keep proper intervals between chambers with allergens, because thermal positive reaction to allergen is generally larger than the area of incubation on the skin while skin reaction never exceeds this area and when strong reaction occurs thermal response might cover weak reaction from neighbour allergens. Thermal stabilization is important as well, because sweaty skin on the back also covers thermal reaction to allergens. It was observed that the problem of sweat is not so significant in case of application on the arms.

Another conclusion is that thermal imaging camera used for this application should have nearer focus range and smaller field of view because it enables more precise analysis of examined skin surface. It has been taken into consideration during development of the measurement stand. The geometric calibration of infrared thermography

system is needed to remove lens distortion from acquired IR images. For further research it is planned to create network-centric system to storage thermographs with physician description (diagnosis), case record, diagnostic results and description parameters. Those thermal images will be classified due to type of diagnosed pathology.

Medical thermal image processing is field of study which should be developed in the future, because it may significantly improve on skin tests assessment. The acquired images later will be analysed in ThermoAnalysis software, with the use of Pulsed Phase Thermography (PPT) to precise recover the gradient distribution of the thermal changes. It can be a valuable additional method in allergology, however it cannot substitute standard visual evaluation of patch tests. Presented results are first stage of longer research process.

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