

Luigi LAINO
Aldo DI CARLO

The San Gallicano Dermatological Institute
for Research and Care, IRCCS,
Via Elio Chianesi 53, 00144 Rome, Italy

Reprints: L. Laino
<laino@ifo.it>

Telethermography: an objective method for evaluating patch test reactions

Telethermography (TT) is a non-invasive imaging technique which can be used to evaluate the body's thermal gradients. It has recently been used as a diagnostic tool in many medical fields, especially in the study of the skin and other external organs. We assessed the applicability of TT in the objective evaluation of patch tests in allergic contact dermatitis, where clinical assessment is difficult, especially for atopic or brown-skinned individuals. In 34 individuals with a history of allergy to nickel sulphate (NiSO₄), we applied a patch containing NiSO₄ to the right side of the back and a patch containing 1% sodium-lauryl-sulphate (SLS) to the left side. As a control, we applied a patch containing an irritant (1% SLS) in a second group of 30 non-allergic individuals. A peculiar pattern was found for allergic reactions. This was characterized by a hot area that extended beyond the borders of the patch site and was oriented towards the nearest lymph-node(s), spreading as a hyperthermic line or lines. For the irritant test (SLS), the hot area was limited to the patch area, and the thermal gradients were lower. Thermography can be considered a useful complementary method for the evaluation of patch tests.

Key words: thermography, allergic contact dermatitis, irritant contact dermatitis, patch test

Article accepted on 2/11/2009

Recently, thermography (TT) has been found to be a useful method in diverse medical fields. The innovative method of thermostimulation has improved the accuracy of this technique, providing further possibilities in many clinical and experimental studies, particularly in allergology and dermatology.

Patch testing is a useful paraclinical method for diagnosing contact allergy [1, 2]. Nonetheless, because its evaluation ultimately depends on visual assessment, it remains a basically subjective method [3]. To address this problem, many instrumental methods have been proposed, such as laser doppler, transepidermal water loss, and macro-video assessment [4-9]. However, these methods can be used only to quantify the intensity of the visible reaction, by measuring, for example, the degree of redness or blood flowmetry; thus they do not allow an allergic response to be distinguished from an irritant response in the evaluation of patch tests. This is a frequent problem in allergology facilities, and it often constitutes an obstacle to evaluating patch-test reactions in, for example, atopic or brown-skinned individuals.

Telethermography (TT) is a new technique that reveals the body's caloric emission as infrared radiation and reproduces it on a video-monitor as thermal gradients [10, 11]. In the black and white version, the caloric emission appears as thousands of thermal points whose brightness increases with emission (*i.e.*, brighter = hotter), whereas in the colour version, the caloric emission is seen as 7-10 bands of different colours, each of which corresponds to a different isotherm (*e.g.*, white band = hottest, black band = coldest).

The sensitivity of the thermographs varies from 0.1 °C to > 10 °C. In some studies, the patch area appeared to be "hot" for positive allergic reactions, with the borders of this hyperthermic area extending beyond the clinical borders of the patch. For a positive irritant response, the patch area appeared less hot and did not extend beyond the clinical borders [12-15]. To better evaluate the effectiveness and applicability of this technique in evaluating patch tests, we compared the results of a nickel sulphate (NiSO₄) patch test (as an allergy test) to those of a sodium lauryl sulphate (SLS) patch test (as an irritant test).

Materials and methods

We enrolled two groups of individuals. The first group included 34 Caucasian individuals (19 females and 15 males, aged 23-62 years) who in the period 2005-2007 had been examined at our allergology facility and were found to have been allergic to NiSO₄ according to the GIRDCA series patch test. The second group consisted of 30 individuals (16 females and 14 males, aged 21-58 years) who had been seen at our facility in the same period and who were not allergic to NiSO₄ according to the GIRDCA series patch test. All participants provided written informed consent. The study was performed between 2005 and 2008.

In the first group, a standard 5% NiSO₄ patch test (GIRDCA series) was applied to the right side of the upper back. The next day, a patch containing 1% SLS

was applied to the left side of the upper back, symmetrically. The two patches were removed at the same time, so that the NiSO₄ patch remained for 48 hours and the SLS patch for 24 hours. For the second group, a 1% SLS patch was applied to the left side of the upper back for 24 hours.

The evaluation of patch tests was performed 30 minutes after patch removal, both clinically and by TT. The clinical evaluation was based on the criteria of the International Contact Dermatitis Research Group (ICDRG) [1, 9]. For the thermographic evaluation, we used, indifferently, AGEMA Thermovision 880TM, AGA Thermovision 660TM, or FLIR3000 ThermocamTM. To improve the sensitivity of the TT (≥ 0.1 °C), we used the thermostimulation method, in accordance with Ippolito and Di Carlo [15]. In brief, this method entails evaluating, instead of the thermal gradients, their corresponding times of thermal recovery (TRT) after thermal stimulation at 5 °C $\times$ 20", using a special thermal probe. This method

allows difficulties in evaluating very low thermal gradients (*e.g.*, < 0.01 °C) to be overcome [18-20]. All data were recorded in a single database.

Results

Allergic response

All 34 individuals belonging to the first group (*i.e.*, those with a history of allergy to NiSO₄) showed a positive reaction to NiSO₄, with a clinical score that varied from "+" to "++++" (*table 1*). In all of these individuals, TT showed a hot area which extended beyond the visible borders of the patch site, forming a sort of hyperthermic "halo". This was asymmetrically oriented towards the nearest lymph-node(s), spreading as one or more hyperthermic lines (*figure 1, right; figure 2*). Considering the hottest point of the perilesional area, the hyperthermal gradient had a mean Δt of

Table 1. Reaction to allergic patch tests for NiSO₄ (n = 34 individuals)

Participant	Clinical score (*)	Δt (°C)	Hyperthermic lymphocentric line	Cold centre
1.	+++	2.5	Yes	No
2.	+++	3.2	Yes	Yes
3.	++	2.4	Yes	No
4.	++	1.4	Yes	No
5.	++++	2.8	Yes	Yes
6.	+++	2.5	Yes	No
7.	+++	2.5	Yes	No
8.	+	1.8	Yes	No
9.	+	1.6	Yes	No
10.	++	2.4	Yes	Yes
11.	++	2.2	Yes	No
12.	++	1.3	Yes	No
13.	++	1.5	Yes	Yes
14.	+	1.8	Yes	Yes
15.	++	2.6	Yes	No
16.	++	1.8	Yes	No
17.	+++	2.6	Yes	No
18.	+++	2.5	Yes	Yes
19.	+	0.8	Yes	No
20.	+	1.6	Yes	No
21.	++	1.5	Yes	No
22.	++	1.8	Yes	No
23.	+++	2.5	Yes	No
24.	++	1.5	Yes	No
25.	+++	1.6	Yes	No
26.	+++	2.2	Yes	Yes
27.	++++	2.8	Yes	Yes
28.	+++	1.8	Yes	No
29.	+++	1.4	Yes	Yes
30.	+++	1.8	Yes	No
31.	++	2.5	Yes	No
32.	++++	2.6	Yes	No
33.	+++	1.7	Yes	No
34.	++	2.2	Yes	No

*Based on the criteria of the International Contact Dermatitis Research Group.

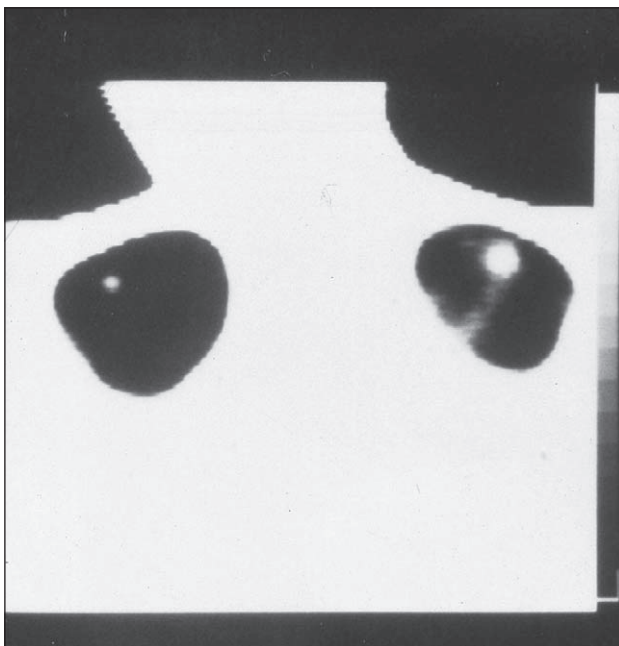


Figure 1. Participant 4. Double patch test in a person allergic to NiSO₄; left side: irritant (SLS); right side allergen (NiSO₄). Note, thermographically, on the right side, the hyperthermal halo and its lymphocentric pseudopod.

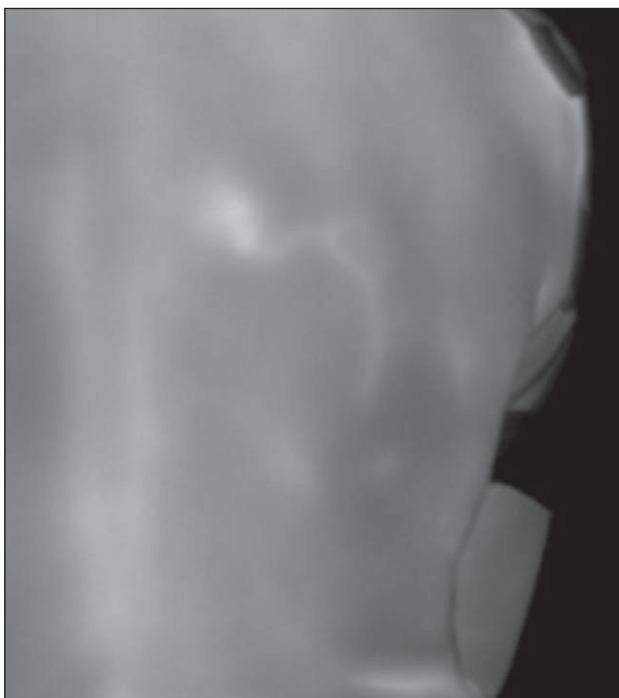


Figure 2. Participant 8. Thermography of an allergic patch test to NiSO₄. Note the presence of halo and of the lymphocentric stria.

2.02 °C. In 9 of the 34 individuals, a cold centre was present at the patch site of the patch, whereas the perilesional hyperthermia was constantly present (figure 3).

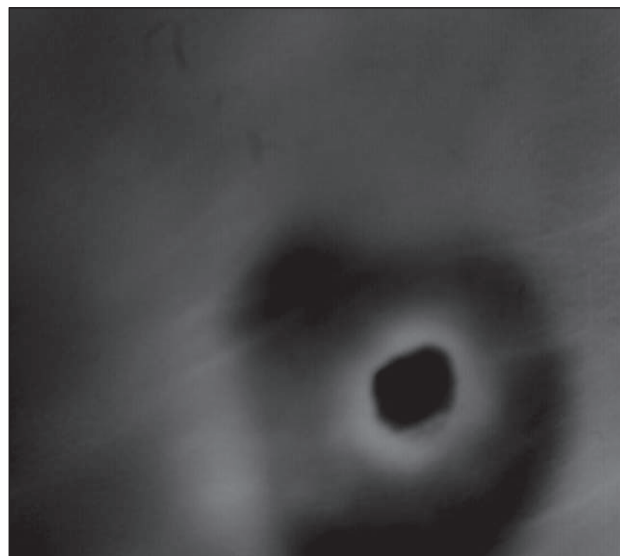


Figure 3. Participant 10. Telethermography of an allergic patch test to NiSO₄. Initial blistering inside the patch area. Note the persistence of the “halo”.

Irritant response

Upon visual examination, a clinical reaction to 1% SLS was found for 41 (64%) individuals: 22 (64%) individuals in the first group and 19 (63%) individuals in the second group (table 2). Objectively, the patch area was weakly erythematous or vesicular. When performing TT, in many cases the patch site appeared to be hot, though the hyperthermic gradients were lower (Δt = mean 0.95 °C) than those found for the NiSO₄ patch test (Δt = 2.02 °C) ($p < 0.01$, Student's test). Moreover, in contrast to the pattern observed for the NiSO₄ patch test, in no case did the hyperthermic area extend beyond the borders (figure 1, left). Furthermore, a cold centre was observed in 23 (36%) of the 64 individuals, probably due to an initial blistering in the patch site. This fact was observed more frequently than for NiSO₄ patch test (9/34, 27%) (figure 4).

Discussion

Because the evaluation of patch tests depends on visual assessment, it is mainly subjective and easily leads to “false-positive” or “false-negative” results. Moreover, in atopic individuals and persons with dark brown skin, an accurate evaluation can be even more difficult. To address these pitfalls, we used TT, which allowed us to overcome the problems inherent to traditional thermometric methods, which require primary point detection and the reassembling and composing of a “thermal map”. TT simultaneously detects thousands of thermal points of the caloric source (in this case the human body) and instantly transforms them into punti-form video-signals (pixels), which form a characteristic picture on the monitor in either grey tones or colour (the “infrared man”). Thus TT has the advantages of both immediately identifying “hot” or “cold” spots and revealing patterns that are specific to the two types of reactions (*i.e.*, allergic *versus* irritant) [16, 17]. TT could be applied in the study of not only skin but also

Table 2. Reaction to irritant patch tests for SLS (n = 64 individuals)

Participant	Clinical score*	Δt (°C)	Hyperthermic lymphocentric line	Cold centre
Study group (history of allergy to NiSO₄)				
1.	+	1.2	No	No
2.	+	0.6	No	No
3.	+	0	No	Yes
4.	+	0	No	Yes
5.	+	0.5	No	No
6.	+	0.5	No	No
7.	+	0.8	No	Yes
8.	+	0	No	No
9.	+	1.1	No	No
10.	+	2.2	No	No
11.	+	1.3	No	No
12.	+	0.5	No	No
13.	+++	0	No	Yes
14.	+++	0	No	Yes
15.	++	0	No	Yes
16.	++	0	No	Yes
17.	+++	0.6	No	No
18.	+++	0.8	No	No
19.	+++	1.0	No	No
20.	+	0	No	Yes
21.	+	1.8	No	No
22.	++	2.0	No	No
23.	++	1.5	No	No
24.	++	0.6	No	No
25.	++	0.1	No	No
26.	+	2.0	No	Yes
27.	++	0	No	Yes
28.	+	0	No	Yes
29.	+	0	No	Yes
30.	++	0.5	No	No
31.	+	0.6	No	Yes
32.	++	0.7	No	Yes
33.	++	2.2	No	Yes
34.	+	0.3	No	No
Control group (no history of allergy to NiSO₄)				
35.	+	0.6	No	No
36.	+	0.4	No	No
37.	+	0.8	No	No
38.	+	0.5	No	No
39.	++	0-	No	Yes
40.	+++	0-	No	Yes
41.	++	2.2	No	Yes
42.	++	0.3	No	Yes
43.	+	0.4	No	No
44.	+	0.8	No	No
45.	+	0.5	No	No
46.	+	1.2	No	No
47.	+++	0	No	Yes
48.	+++	0	No	Yes
49.	+	0.3	No	No
50.	+	0.8	No	No
51.	+	0.8	No	No
52.	+	0.5	No	No
53.	+	0.6	No	No

(continued)

Table 2 (continued)

Participant	Clinical score*	Δt (°C)	Hyperthermic lymphocentric line	Cold centre
54.	+	0.7	No	No
55.	++	2.0	No	No
56.	+++	0.3	No	Yes
57.	+	0.4	No	Yes
58.	+	0.8	No	No
59.	+	0.5	No	No
60.	+	0.6	No	No
61.	+	0.7	No	No
62.	+	1.5	No	No
63.	+++	1.5	No	No
64.	+++	1.4	No	No

*Based on the criteria of the International Contact Dermatitis Research Group.

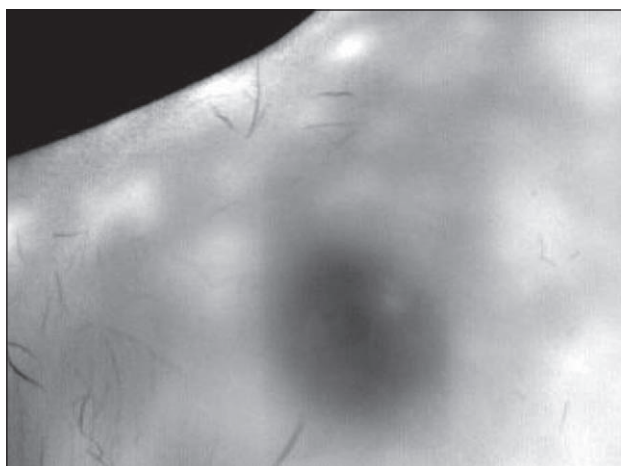


Figure 4. Participant 2. Telethermography of an irritant patch. Note the cold centre due to initial blistering in the patch area and the absence of the “halo”.

the mammary organ, the osteo-articular apparatus, the peripheral nervous system, external genitalia, and superficial vessels. Finally, to better evaluate thermal gradients in the dermatological field and in the study of patch testing, we used the thermal stimulation technique, which allows the problem of weak positive reactions ($\Delta t < 0.1$ °C) to be overcome [13, 14].

Conclusion

TT can be considered as an objective, reproducible and non-invasive method for evaluating patch tests, allowing for the definition of a thermographic pattern of allergic contact hypersensitivity, which can be distinguished from the pattern of irritant hypersensitivity, as indicated by Baillie, who first applied this technique and defined the pattern of allergic tests [14]. This method is also rapid and easy to perform and could be of great use not only in allergology but also in other areas of dermatology [15].

We are currently planning a study to better understand the mechanisms that could explain the asymmetric perilesional hyperthermia of the allergic patch and its spreading

along lymph-centric line(s). We originally believed that this simply could have been a “thermal flame” or a “chimney”, yet we realised that this is not very plausible because the hyperthermic line is clearly directed toward the nearest lymphnode(s) and does not follow a gravitational pathway. Similar hyperthermic lines or *striae* have been observed in cases of nodular melanoma [15]. We believe that the hyperthermia of these *striae* is correlated with an immuno-mechanism, as supposed by Baillie [14, 15]. In this regard, it will be necessary to study the cellular immunocompetent populations in the patch area (e.g., CD4+, CD8+ lymphocytes, Langerhans cells) and related oxidative reactions [21-25]. To confirm this, an extensive immunohistochemical study needs to be performed. ■

Acknowledgements. The authors would like to express their gratitude to Dr. Antonio Cristaudo, Department of Allergic, Ambient and Professional Dermatology, Dermatological Institute of San Gallicano for Research and Care, Rome, for his kind contribution to the allergometric evaluation of our patients. We would also like to acknowledge Miss Paula Irene Franke for revising the manuscript. The authors declare that they have no conflict of interest in this original article.

References

1. Lachapelle JM, et al. Proposal for a revised international standard series of patch tests. *Contact Dermatitis* 1997; 36: 121-3.
2. Belsito DV. Patch testing: after 100 years, still the gold standard in diagnosing cutaneous delayed-type hypersensitivity. *Arb Paul Ehrlich Inst Bundesamt Sera Impfstoffe Frankf A M* 1997; 91: 195-202.
3. Mowad CM. Patch testing: pitfalls and performance. *Curr Opin Allergy Clin Immunol* 2006; 6: 340-4.
4. Zuang V, Archer G, Rona C, Vignini M, Mosca M, Berardesca E. Predicting visual assessment of allergic patch test reactions by non-invasive measurements. *Skin Pharmacol Appl Skin Physiol* 2000; 13: 39-51.
5. Bjarnason B, Flosadóttir E, Fischer T. Objective non-invasive assessment of patch tests with the laser Doppler perfusion scanning technique. *Contact Dermatitis* 1999; 40: 251-60.
6. Nyrén M, Kuzmina N, Emtestam L. Electrical impedance as a potential tool to distinguish between allergic and irritant contact dermatitis. *J Am Acad Dermatol* 2003; 48: 394-400.

7. Goon AT, Leow YH, Chan YH, Goh CL. Correlation between laser Doppler perfusion imaging and visual scoring of patch test sites in subjects with experimentally induced allergic and irritant contact reactions. *Skin Res Technol* 2004; 10: 64-6.
8. Schuster C, Kränke B, Szolar-Platzer C, Aberer W. Macro-video documentation patch tests. *Contact Dermatitis* 2005; 52: 177-83.
9. Fullerton A, Stücker M, Wilhelm KP, *et al.* Guidelines for visualization of cutaneous blood flow by laser Doppler perfusion imaging. *Contact Dermatitis* 2002; 46: 129-40.
10. Stüttgen G, Flesch U, Witt H, Wendt H. Thermographic analysis of skin test reaction using AGA thermovision. *Arch Dermatol Res* 1980; 268: 113-28.
11. Kaliuzhnaia LD. The use of thermography for the objective assessment of treatment efficacy for atopic dermatitis patients. *Vrach Delo* 1990: 88-90.
12. Raskin MM, Zies PM. Role of thermography in allergic contact dermatitis. *Contact Dermatitis* 1977; 3: 206-7.
13. Agner T, Serup J. Contact thermography for assessment of skin damage due to experimental irritants. *Acta Derm Venereol* 1988; 68: 192-5.
14. Baillie AJ, Biagioni PA, Forsyth A, Garioch JJ, Mcpherson D. Thermographic assessment of patch-test responses. *Br J Dermatol* 1990; 122: 351-60.
15. Di Carlo A. Thermography and the possibilities for its applications in clinical and experimental dermatology. *Clin Dermatol* 1995; 13: 329-36.
16. Hardy JD, Gagge AP, Stolwijk AJ. *Physiological and behavioural temperature regulation*. Springfield: Thomas, 1970.
17. Hardy JD. The radiating power of human skin in the infrared. *Am J Physiol* 1939; 127: 454-62.
18. Holti G, Mitchell KW. Estimation of the nutrient skin blood flow using a segmented thermal clearance probe. *Clin Exp Dermatol* 1978; 3: 189-98.
19. Cary J, Kalisher L, Sadowsky N, Mikic B. Thermal evaluation of breast disease using local cooling. *Radiology* 1975; 115: 73-7.
20. Brooks PG, Heldfond AJ, Margolin ML, Allen AS, Gart S. Graphic stress telethermometry. An ideal office screening device for the detection of breast disease. *J Reprod Med* 1980; 25: 1-4.
21. Saint-Mezard P, Krasteva M, Chavagnac C, *et al.* Afferent and efferent phases of allergic contact dermatitis (ACD) can be induced after a single skin contact with haptens: evidence using a mouse model of primary ACD. *J Invest Dermatol* 2003; 120: 641-7.
22. Saint-Mezard P, Berard F, Dubois B, Kaiserlian D, Nicolas JF. The role of CD4+ and CD8+ T cells in contact hypersensitivity and allergic contact dermatitis. *Eur J Dermatol* 2004; 14: 131-8.
23. Bos JD, Teunissen MB, Kapsenberg ML. Immunology of contact dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1989; 151: 84-87; discussion 106-10.
24. Kanerva L, Estlander T, Ranki A. Lymphocytes and Langerhans cells in allergic patch tests. *Derm Beruf Umwelt* 1987; 35: 17-9.
25. Kanerva L, Ranki A, Lauharanta J. Lymphocytes and Langerhans cells in patch tests. An immunohistochemical and electron microscopic study. *Contact Dermatitis* 1984; 11: 150-5.