

The Longest Wheal Diameter Is the Optimal Measurement for the Evaluation of Skin Prick Tests

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Key Words

Wheal and flare reactions · Skin prick test · Wheal diameter

Abstract

Background: Mean diameter or longest diameter are the 2 most frequently used parameters for wheal response assessment after skin prick testing (SPT). We aimed to compare these 2 parameters taking as gold standard the surface of the wheal skin response. **Patients and Methods:** Patients suspected of having an allergic reaction against inhalant allergens have been skin prick tested using the Pan-European GA²LEN SPT panel. Fifteen minutes later, macroscopically evident wheal and flare reactions were marked with a pen and transferred to paper with a transparent scotch tape. Each paper-transferred wheal was scanned with an ordinary scanner, and its surface-corresponding maximum perpendicular diameters and longest diameters were measured using a computer software application for image recognition, developed for this purpose. Correlation coefficients (Spearman's ρ) between surfaces and respective mean (ρ_{mean}) or longest (ρ_{longest}) diameters were calculated and subsequently compared. **Results:** 1,554 SPTs were performed in 74 pa-

tients. In 264, a macroscopically evident wheal and flare response was observed. Both mean and longest diameters correlated significantly with the wheal surfaces. However, ρ_{longest} was statistically significantly larger than ρ_{mean} when the surface of the wheal was $>17 \text{ mm}^2$ ($\rho_{\text{longest}} > 0.860$ vs. $\rho_{\text{mean}} < 0.660$; $p < 0.05$). Such a surface corresponds to a maximum diameter of approximately 7 mm and a mean diameter of approximately 6 mm. Thus, the larger the surface of the wheal, the more appropriate the usage of the longest diameter. **Conclusions:** The longest wheal diameter alone seems to be a better surrogate marker of the wheal surface in comparison with the mean diameter. In addition, it is easier and faster to measure. Therefore, we propose this as the optimal methodology to evaluate SPTs.

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Introduction

Standardization of skin prick tests (SPTs) is necessary in order to optimize their performance [1, 2]. Although factors related to the extracts and allergen panel have been extensively described [2], the measurement proce-

Table 1. Spearman's correlation coefficients for mean and longest diameter for different wheal surface values

Wheal surface cutoff values	Spearman's correlation coefficients between surface and		Number of observations	p value ^b
	mean diameter	longest diameter		
>0 mm ²	0.933 (0.915–0.947)	0.951 (0.938–0.962)	264	0.523
>6.271 ^a mm ²	0.857 (0.804–0.897)	0.861 (0.809–0.900)	132	0.400
>15 mm ²	0.731 (0.593–0.828)	0.882 (0.809–0.928)	60	0.337
>17 mm ²	0.651 (0.466–0.781)	0.864 (0.776–0.918)	55	0.046
>20 mm ²	0.697 (0.517–0.818)	0.866 (0.773–0.922)	49	0.032

Figures in parentheses are 95% confidence intervals. All Spearman's correlation coefficients were statistically significant with a p value <0.001.

^a Median wheal surface of the sample examined.

^b Comparisons are based on Chow's test after ordinary least squares regression on the separate measured lengths and the respective surfaces.

ture has not received adequate attention. It is generally accepted that the most accurate way to assess a wheal response is planimetry (either direct or from a traced copy), since it includes all the information (surface) of different shapes that may have resulted [3]. However, it is difficult to perform manually, time consuming and rather expensive to measure automatically using more sophisticated techniques [4].

A recent practice parameter has proposed different approaches that can be used in this respect. These include the mean wheal diameter $[(D + d)/2]$, where D = the longest diameter of the wheal, and d = the longest diameter orthogonal to D , the longest diameter alone, planimetry or semiquantitative methods like the comparison of the area of the allergen-induced wheal reaction with that of the positive control (either histamine dihydrochloride or codeine phosphate) [1].

Semiquantitative method measurements are influenced by substantial parameters such as the substance used (histamine dihydrochloride or codeine phosphate) [5], the concentration (e.g. 1 or 10 mg/ml histamine dihydrochloride) and the degree of the skin reactivity [6]. Therefore, even small differences in size generate large differences in sensitivity which afford this method poor precision [6]. For routine use, mean or longest diameters are most convenient, easy and cheap to apply since only a pen and ruler are needed. In the literature, there is no information on whether any of these methods has characteristics that would render it preferable to the other.

We aimed to compare the mean wheal diameter with the longest diameter alone, taking as gold standard the surface of the wheal skin response.

Patients and Methods

Patients suspected of having an allergic reaction against inhalant allergens have been skin prick tested using the same technique (pricking with a lancet at the volar surface of the forearm) and extracts [cat, dog, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blatella*, tree mix Northern (birch, hazel, alder), olive, cypress, plane, grass mix, *Artemisia*, *Ambrosia*, *Parietaria*, *Alternaria*, *Cladosporium*, *Aspergillus*] of the Pan-European GA²LEN SPT panel [2]. Fifteen minutes after SPT, macroscopically evident wheal and flare reactions were marked with a pen (width of stroke 0.3 mm) and transferred to paper with a transparent scotch tape. The paper-transferred wheals were scanned with a Hewlett-Packard PSC 1510 scanner. A computer software application for image recognition from the scanned paper [implemented in C (programming language) and compiled by GCC (GNU C Compiler) of DJGPP 2.03 (computer operating system) environment] was developed to estimate the surface of each scanned wheal and its corresponding longest diameter and maximum perpendicular diameters. The accuracy of the program was evaluated by measuring surfaces with known characteristics (e.g. circles, ellipses, polygons and other complex schemas with given radius, sides and angles needed to calculate the exact surface) and found to be 0.0001 mm for lengths and 10^{-6} mm² for surfaces [standard deviation from the actual (true) value]. Correlation coefficients (Spearman's ρ) between surfaces and respective mean (ρ_{mean}) or longest (ρ_{longest}) diameters were calculated and subsequently compared.

Results

1,554 SPTs were performed in 74 patients. In 264, a macroscopically evident wheal reaction (all visible wheals that could be easily marked with a pen) was observed. The median (interquartile range) values were 6.271 (11.546) mm² for the surface of the wheal responses, 3.932

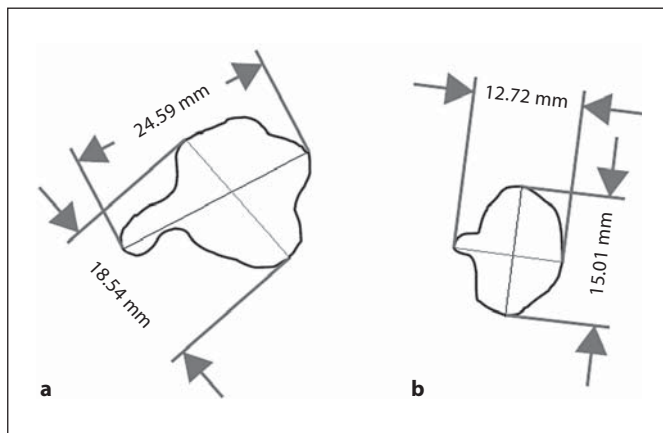


Fig. 1. Assessment of the longest diameter in cases of wheal skin responses with pseudopodia. **a** In this case, the longest diameter (24.59 mm), part of which is included in the pseudopodium (18.54 mm), is the longest, rather than the one measured as if there was no pseudopodium (18.54 mm). **b** On the contrary, in this case, the longest diameter is similar to that measured as if there was no pseudopodium (15.01 vs. 12.72 mm).

(2.17) mm for the mean diameter and 5.83 (3.759) mm for the longest diameter. Spearman's ρ correlation coefficients between mean or longest diameters and respective surfaces are presented in table 1. Generally, both mean and longest diameters correlated significantly with the wheal surfaces. However, ρ_{longest} was statistically significantly larger than ρ_{mean} when the surface of the wheal was $>17 \text{ mm}^2$ ($\rho_{\text{longest}} > 0.860$ vs. $\rho_{\text{mean}} < 0.660$; $p < 0.05$). Such a surface corresponds to a maximum diameter of approximately 7 mm and a mean diameter of approximately 6 mm. Namely, the larger the surface of the wheal, the more appropriate the usage of the longest diameter alone.

Discussion

All measurements were evaluated as independent since we were interested in the responses themselves rather than in their origin. Thus, any within-subject correlation was irrelevant to the outcome of interest. Alternatively, we could use a sample of randomly selected simple closed curves but we preferred the clinical practice realization example.

Comparison of the measured and the predicted surfaces from the available parameters [$\pi(D/2)^2$ for circle-resembling reactions and $\pi(D/2)(d/2)$ for ellipse-resembling wheal reactions] reveal that only a few reactions resemble an ellipse (only 10/264) and none of them a circle. On the contrary, the large observed deviations between the predicted and the calculated surfaces could be explained by the fact that most wheal reactions were irregular ellipsoid or irregularly closed curves generated from an ellipsoid pattern. Macroscopically, most of them did have smaller or larger segments deviating smoothly from the main ellipsoid trajectory to form small conic sections. In cases of pseudopodia, the longest diameter could include the pseudopodia in the measurement of the longest diameter (fig. 1).

These results correspond to computerized measurements; further bias would be expected to occur in manual measurements additional to the longest diameter like the identification of the maximum perpendicular diameter and the formation of the right angle (90°) between them.

In conclusion, the longest wheal diameter alone is not only a better surrogate marker of a wheal surface, in comparison with the mean diameter, but also easier and faster to measure. Therefore, it seems to be preferable for SPT evaluation.

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