

Brief communication

Computerized measurement of allergen-induced skin reactions

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The areas of 50 randomly chosen skin-test reactions were measured with a graphics tablet interfaced to a microcomputer. The computer-determined areas were compared with the sums and products of orthogonal diameters, the maximum diameter, and the actual areas of the reactions. The areas measured by the computer were highly correlated with the actual areas ($r = 0.999$). Both the sums and products of orthogonal diameters were also highly correlated with the actual areas ($r = 0.953$ and $r = 0.988$, respectively) and added little to the correlation of the maximum diameter ($r = 0.923$). The average coefficient of variation for repeated computer area measurements was 5.3%. Area and maximum diameter measurements were then compared in a study designed to evaluate the variation of prick tests applied by different persons. Area measurements revealed significant differences between the testers, which were not found when maximum diameter measurements were compared. Computerized area determination is a rapid, accurate means for quantitating skin-test reactions. The precision offered by this method is of potential importance for studies involving quantitative skin testing. (J ALLERGY CLIN IMMUNOL 69:536, 1982.)

Quantitative skin testing is a frequently employed procedure in allergy research.¹ It provides a means for comparing the biologic potencies of allergen extracts² and a standard for in vitro assays of extract potency.³ Variations of this technique have also been used for evaluating the effects of drugs on the allergic response and for comparing the sensitivities of subjects in clinical studies.^{4, 5} Despite this popularity, there is no uniformly used method for measuring skin-test reactions. The commonly used methods estimate the area of the reaction. Actual area measurements have been difficult to obtain because of the irregular shape of reactions. The clinically useful system of scoring reactions from 1 to 4+ is not precise enough for these purposes.

The ability of a graphics tablet to rapidly convert the irregular shape of a skin-test reaction into digital data suitable for computer analysis offers a new method for quantitating skin reactions. This study compared computer-derived skin-test areas with the actual areas of the reactions and with several commonly used methods for estimating area. Area measurements were then compared with maximum diameter measurements to evaluate two sources of prick skin-test variation.

METHODS

Fifty outlines of wheal responses were randomly selected from approximately 800 recorded during skin-test titrations on ragweed-sensitive subjects (Fig. 1). The responses had been recorded by outlining the wheal with a fine, porous-tip pen. Translucent tape was then applied, picking up the ink outline. The tape was then removed and placed on data sheets. The selected wheal outlines were collected onto a single sheet by tracing, and multiple copies were made with a copy machine.

The actual areas of the wheals were determined by carefully cutting and weighing each wheal outline in triplicate. The weight per unit area of copy machine paper was determined for areas ranging from 25 to 2100 mm². The average

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TABLE I. Comparison of area and diameter measurements

	Area (mm ²)	Maximum diameter (mm)
Location		
Proximal	717	35.75
Mix-proximal	719	35.56
Mid-distal	704	34.69
Distal	589	32.19
p value*	0.351	0.236
Tester		
A	597†	33.12
B	718	33.75
C	814†‡	35.38
D	600‡	35.94
p value*	0.026	0.432

*Probability that the four means are equal by analysis of variance.

†Values significantly different, $p = 0.004$, Student's *t* test.

‡Values significantly different, $p = 0.014$, Student's *t* test.

coefficient of variation was 2.1% for repeated weighings of the same sample and 2.6% for weighing of different samples of a wheal outline.

Three observers independently measured each outline for the maximum diameter and the longest diameter perpendicular to the maximum diameter. An Apple Graphics tablet interfaced to an Apple II microcomputer was used for computer measurements of the wheal areas. The results were directly displayed in square millimeters.

For experimental design purposes we wished to compare the variation of different skin-test sites on the volar forearm with that produced if the prick tests were applied by different individuals. Histamine phosphate (1 mg/ml) was selected as the skin-test material. By definition this concentration of histamine should produce a 3+ reaction. Four individuals (three experienced nurses and one allergy fellow) each applied a set of four prick tests to the forearms of four nonallergic, young adult, male volunteers. Each set of tests was arranged as a column between the antecubital fossa and wrist. All tests were placed at least 5 cm from all other tests. The location of the set of tests, right or left arm, radial or ulnar side, was determined by a randomized Latin square design. The outlines of the flare responses were recorded and measured as described above.

RESULTS

As expected, the area as determined by the microcomputer agreed extremely well with that determined by weighing ($r = 0.999$). There was no detectable bias, and the variation of both methods increased at an equal rate as the areas became very small. The average coefficient of variation for the computer measurements was 5.3%. The maximum was 16.5% for areas less than 20 mm². The time required for the computer measurements was less than

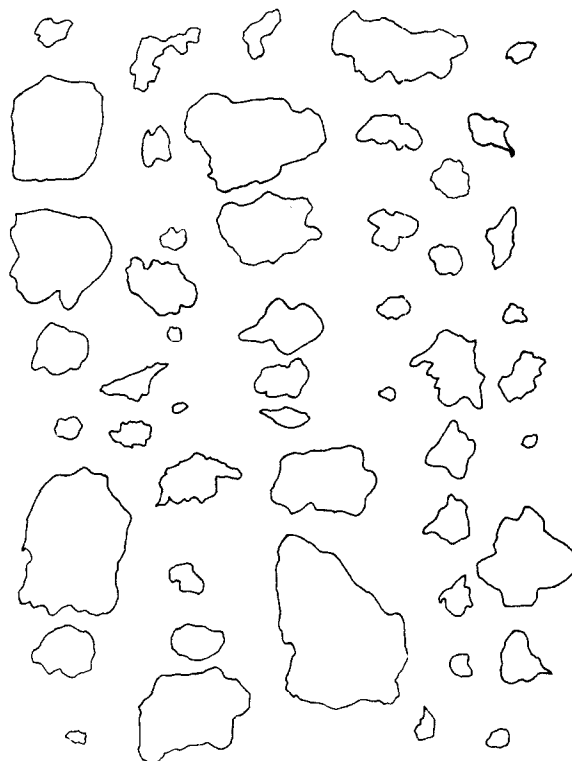


FIG. 1. Outlines of the 50 wheal areas used for study. The areas range from 10.9 to 1225.9 mm².

one-tenth the time required for cutting and weighing equal number of samples.

Measurements of the diameters correlated surprisingly well both with the areas and between the three observers. The correlation between the three observers for the longest diameter, the sums of the diameters, and the products of the diameters are all greater than 0.985. The product of the diameters correlated best with the area (mean for three observers, $r = 0.988$) but was little better than the average correlations for the diameter sums ($r = 0.953$). The longest diameter also correlated well with area ($r = 0.932$).

The results of the prick skin-test experiment are shown in Table I. The diameters and areas observed were approximately normally distributed. Analysis of variance revealed no significant differences between the means of the area and the diameter measurements of the four forearm locations. Significant differences were found when the mean flare areas produced by the four individual testers were compared ($p = 0.026$ by analysis of variance). These differences between the mean responses produced by the four individual testers cannot be demonstrated with the means of the maximum diameter measurements ($p = 0.432$).

DISCUSSION

The previously reported methods of either summing or multiplying the diameters of skin reactions^{6, 7} both correlated well with the actual area of the reactions as did simple measurement of the longest diameter. The advantage of these methods is that measurements can be rapidly made directly from the patient's skin. The diameter measurements were also reproducible from one observer to another.

The graphics tablet-microcomputer combination proved to be a rapid and precise method for measuring actual skin-test areas. Although the precision offered by area measurements is not needed in clinical practice, it can reveal differences that might otherwise be missed in experimental studies. The increased sensitivity of area measurements was seen in the prick-test study. Comparison of the skin responses produced by the four testers revealed significant differences when area measurements were used but not when maximum diameter measurements were used. Computerized area measurements thus offer a rapid and precise means of measuring the size of immediate skin tests for studies in which this degree of precision is necessary.

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