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BRIEF RESEARCH REPORT

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The shape of and applied weight on skin prick lancets critically affect the wheal size in the skin prick test

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ABSTRACT

The global application of the skin prick test (SPT) is attributed to the low costs, easy execution, and *in vivo* approach. Still, the healthcare professionals' technique and the lancet shape may challenge the standardization of the method. Thus, we investigated the influence of the shape of the lancet and the applied weight on the wheal size of SPT. Two allergic and one non-allergic individual were tested with allergens (*Dermatophagoides pteronyssinus* and *Phleum pratense*) and histamine solution (positive control), respectively. Horizontally (HS) and diagonally (DS) shouldered lancets with the same tip length (1 mm) were tested under two different conditions: either 60 g or 120 g weight pressure. The wheal size induced by the 4 different combinations was measured. The higher-weight device (120 g) induced a significantly larger and less variable wheal response with the tested allergens and histamine. However, the shape of the lancet affected the wheal size more than the applied weight. The least variable response was measured to histamine for the horizontal-shouldered lancet combined with the higher weight, whereas the same lancet with the lower weight resulted in a significant number of false negative results.

Keywords: Skin prick test, Allergen, Prick test lancet, Standardization, Methodology

Allergy diagnosis is based on detailed clinical history, sensitization profile using skin prick test (SPT), and/or allergen-specific IgE (sIgE) test, and, if needed, organ challenge tests. The SPT method provides the physiological aspect of the allergic response by producing a wheal and flare skin response that can be measured. An EAACI survey conducted in 31 countries depicted SPT as the primary diagnostic method utilized in $^{2}/_{3}$ of all allergic diseases and in 90% of inhalant allergies.[1] The SPT is an inexpensive, safe method producing immediate results. Though, the reproducibility of the results relies on the operator's technique and the design of the lancet used for administering the allergen.[2,3] Indeed, Andersen et al showed that the wheal size induced by the positive control solution (10 mg/ml histamine) was proportional to the weight applied on the lancet.[4] In addition, several studies focused on the design of the lancet, though none evaluated the result of the combination of the lancet design and applied pressure.[5,6,7] Therefore, in this pilot study, we aimed to investigate the effect on the wheal size

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of two differently designed lancets applied with two different weights for two different allergens and histamine.

One healthy non-allergic control and 2 allergic but otherwise healthy individuals (1 house dust mite, *Dermatophagoides pteronyssinus* (DP), allergic and 1 grass pollen, *Phleum pratense* (PP), allergic) were included in the study conducted from October 2019 to the March 2020. Informed written consent was obtained from participants. Individuals were subjected to 4 rounds of SPT with Soluprick®-products (ALK-Abelló S.A., Madrid, Spain) with at least 1 month's intervals. The SPT was conducted by trained healthcare personnel. The non-allergic individual (age 29) was tested with Soluprick® positive control (10 mg/mL histamine dihydrochloride) (MT 13142) and Soluprick® negative control (MT 13143). The two allergic participants (age 53 and 64, respectively) were tested with the relevant allergen extracts Soluprick® (*Dermatophagoides pteronyssinus* 10 HEP [MT 12764] and *Phleum pratense* 10 HEP [MT 12292]) and positive and negative controls. In each of the 4 rounds, participants were subjected to 4 test series, performed in parallel medially and laterally on the volar side of each forearm by the same operator. Each test series included 1 positive and 1 negative control prick plus 8 pricks with an identical allergen (or histamine in the control person). Tape indicating the number of each prick and providing a fixed spacing between the replicates were placed at the volar part of the forearm 3 cm from the antecubital fossae. Droplets of control and allergen solutions were placed on each side of the tape. Two types of single-headed metal lancets were tested, 1 mm, horizontal shoulders (HS) (Ewo prick lancet, AB Nordic Medifield Serv., Täby, Sweden) and 1 mm, diagonal shoulders (DS) (ALK Lancet, J.N.Eberle Federnfabrik GmbH, Schwabmünchen, Germany) (Fig. 1A). The applied pressure was assured by using devices of defined weights sliding within their handles. Based on the study by Andersen et al, 2 weights were tested, 60 g (60) and 120 g (120) (Fig. 1B). In each round, 4 combinations of lancets and weights were tested: HS-60, HS-120, DS-60, and DS-120. The wheal size was assessed 12 and 15 min after the prick with positive control and allergens, respectively. The edge of the wheal was outlined with a pen, transferred by transparent tape, and

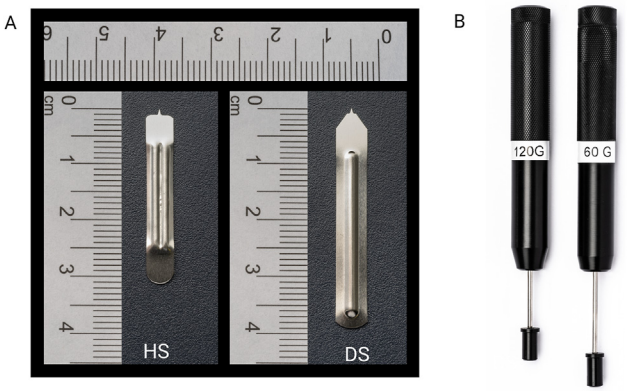

Fig. 1 The design of lancets and weight devices A. Shouldered (left) and diagonal (right) lancets used in the study, B Two weight devices with moveable loads of 120 g (left) and 60 g (right) inside handles

measured (mm^2) with ImageJ 1.49 software. Data were analyzed with GraphPad Prism software, 9.0 (GraphPad Software, La Jolla, USA). The relative variability of the wheal area was expressed as coefficient of variation (CV), calculated as a ratio of standard deviation to the mean.

For the histamine solution, the 120g weight device and the horizontal shouldered lancet induced a wheal area 3 times larger than the same lancet with a 60g weight device (Fig. 2). For the 2 allergens even with the low weight the wheal response induced by the DS lancet was significantly larger than the area induced by the higher weight with the HS lancet (Fig. 2). Whereas, for the diagonal shouldered lancet, the difference between 120g and 60g devices was not statistically significant neither for histamine nor allergens. Importantly based on the 7 mm^2 cut-off, the HS-60 combination (Fig. 2) resulted in 15/32, 12/40, and 5/40 false negative tests for histamine, DP, and PP extracts, respectively, while the HS-120 combination induced wheal response below cut-off in 2 of the 4 positive controls (Fig. 2). Regardless of test substance, most variation was observed for the HS-60 combination (Fig. 2).

This study compared the wheal response induced by 2 commercially available lancets both with similar 1 mm tip but different shoulder shape, using 2 different applied weight conditions. We confirmed the finding by Andersen et al[4] showing a larger wheal response caused by the higher weight when testing the histamine solution and we observed the same phenomenon for 2 allergen extracts, regardless of the

Histamine [mm^2]				D. pteronyssinus [mm^2]				P. pratense [mm^2]				Test substance
HS-120	HS-60	DS-120	DS-60	HS-120	HS-60	DS-120	DS-60	HS-120	HS-60	DS-120	DS-60	Lancet-Weight
21,41	7,13	31,25	24,45	13,8	8,8	29,67	24,86	38,91	17,59	65,59	60,24	Median
24,88%	55,87%	26,49%	28,74%	29,84%	57,72%	29,01%	47,53%	31,70%	72,07%	35,18%	38,38%	CV

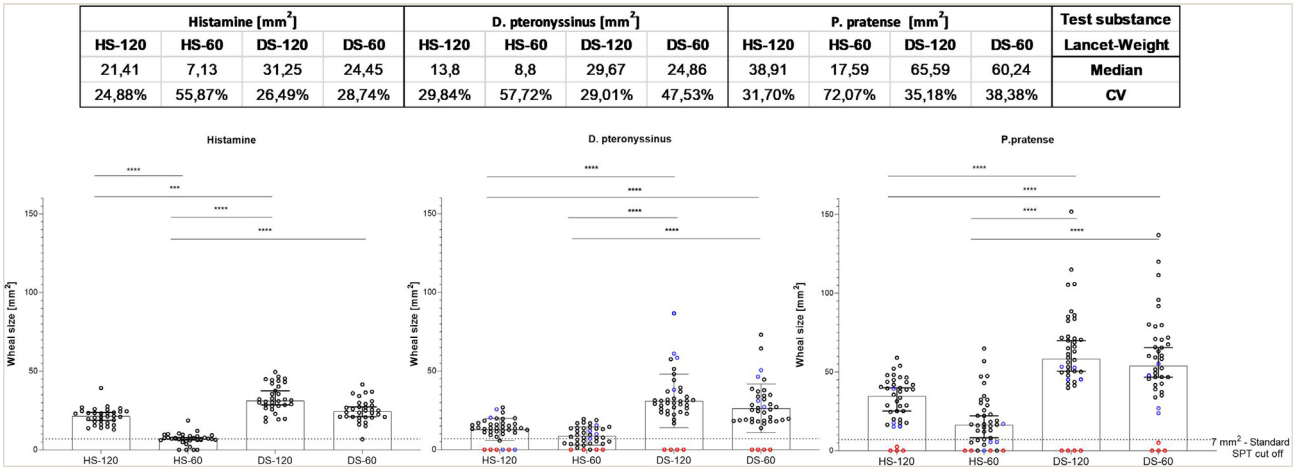

Fig. 2 Effect of lancet/weight combinations on the wheal size. Medians (mm^2) and CV values of wheal area. The horizontal dotted line at 7 mm2 - the standard SPT cut-off; red and blue circles - negative and positive controls. HS and DS - horizontal and diagonal shouldered lancets; 120 and 60–120 g and 60 g weight devices; Statistics: a-c. Kruskal-Wallis test with Dunn's correction, bar graphs - median with 95% CI; two-sided α-level <0.05, (***) $P \leq 0.001$ and (****) $P \leq 0.0001$.

age of participants[8] (Fig. 2). Interestingly, the combination of higher weight and horizontal-shouldered lancet resulted in the least variable response for histamine, and CVs in the lower range for allergens. Less surprisingly, the most significant wheal response independent of the stimulant was induced by the diagonal-shouldered lancet with the higher weight. Although higher weights can be associated with increased bleeding and pain, too low weights can induce false negative values. Indeed, we observed a critical percentage of false negative results while using the lower-weight device to administer histamine and allergen extracts with the horizontal-shouldered lancet. Surprisingly the profile of the 1 mm lancets had a much higher influence on the wheal size than the applied weight. This could be a result of weight distribution, with diagonal-shouldered lancet having shorter surface of contact with a skin, causing concentration of the weight in smaller area and subsequently deeper penetration into the skin compared to the horizontal-shouldered lancet. In our test range even a doubling of the weight could not compensate for the difference in design. This contrasts with a previous study, where the response generated by the diagonal-shouldered lancet was comparable to a horizontal-shouldered lancet. However, in this study the applied pressure was not measured directly but just defined as "moderate" and corresponded to a depression of the skin of 2–3 mm. In addition, the manual reading of the wheal area could have added to the variability of the readouts, as automated skin testing shows more consistency.[9]

Our pilot study was conducted on 3 participants with only 2 applied weights; however, identical locations were chosen in order to reduce the potential bias attributed to differences in skin reactivity. A high number of replicates per each tested condition (n = 32 - histamine and 40 - allergen) intended to increase the strength of the analysis. The results do not allow a precise recommendation of applied weights for the two prick lancets, but at least for the horizontal-shouldered lancet give an indication of a minimal and a too-low weight. Further studies with more participants and several weights would be valuable.

In conclusion, we showed in this study that allergen-specific wheal response depends not only on the weight used during the SPT but to a high degree also on the design of the lancet even if the tip length is the same.

Abbreviations

SPT: skin prick test; DP: *Dermatophagoides pteronyssinus*; PP: *Phleum pratense*; HS: horizontal shoulders; DS: diagonal shoulders; 60: 60g weight device; 120: 120g weight device.

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Data availability statement
Dataset related to this article is accessible after contacting corresponding author.

Authors contributions
Study design – EB, JE, and HM. Methodology - EB, JE, and HM. Experimental part – EB, JE and HM. Data analysis - EB. Data visualization – EB, JE and HM. EB wrote the first draft of the manuscript. All authors revised the manuscript and approved the final version.

Ethics statement
Informed written consent was obtained from participants.

Consent statement
Authors' consent for a publication in WAO. The article is an original work and has not been published and is not considered to be publish elsewhere.

Declaration of competing interest
All authors state no conflict of interest.

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