

5. Aberle SW, Puchhammer-Stöckl E. Diagnosis of herpesvirus infections of the central nervous system. *J Clin Virol.* 2002;25:579-585. doi:10.1016/s1386-6532(02)00037-9
6. Gold JE, Okyay RA, Licht WE, Hurley DJ. Investigation of long COVID prevalence and its relationship to Epstein-Barr virus reactivation. *Pathogens.* 2021;10(6):763. doi:10.3390/pathogens10060763

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

DOI: 10.1111/all.15474

Reliability of a novel electro-medical device for wheal size measurement in allergy skin testing: An exploratory clinical trial

To the Editor,

Skin prick testing (SPT) is the cornerstone of IgE-mediated allergy diagnosis,¹ due to its high sensitivity and specificity.² However, a uniform method for wheal measurement does not exist. Ansotegui et al.² recommends to measure wheals in millimeters with a ruler, in many centers they are outlined with a pen and transfer by tape to a paper and then measured. Subsequently, the specialist is able to manually measure the maximum (MD) and orthogonal diameter (OD) of the wheal. This procedure is time consuming and makes reproducible measurements difficult.^{2,3} Knowing the wheal's area could help make a more accurate diagnosis.⁴ Over the last 30 years, many attempts have been made to develop a device to measure the size of SPT.³ Nexkin DSPT® (Figure S1A,B) is a novel mechatronic system based on 3D laser technology, that automatically locates allergen's wheal and measures its size (MD, OD and area in square millimeters) (Figure S1C).

A prospective clinical trial was conducted at Clínica Universidad de Navarra (NCT05284565) to evaluate the level of agreement in wheal size measures between this new device and the manual procedure, to assess the test-retest reliability for both procedures, and to compare reading value variations between both measurement approaches. Methods details are shown in Appendix S1.

A total of 108 individuals were screened during the study period (Figure S2) and 93 patients were finally included for analysis. SPT was performed with positive (histamine) and negative (saline solution) controls. Fifteen minutes later, two consecutive readings with the device and two manual readings were performed by two separate nurses. Comparisons between first and second readings are shown in Table S1.

Correlations between the manual procedure and the device (Figure 1) showed a relatively strong association, and all of them were statistically significant (Area: $r = .742$, $p < .001$; MD, $r = .700$, $p < .001$; OD, $r = .644$, $p < .001$). The intraclass correlation coefficient (ICC) values showed poor to moderate agreement between the manual procedure and the device [0.49 (95% CI: 0.26–0.65) to 0.70 (95% CI: 0.53–0.81)]. Test-retest reliability (Figure S3) was found to be moderate to good for the manual procedure (ICC values ranged from 0.57 [95% CI: 0.42–0.70] to 0.80 [95% CI: 0.71–0.86], corresponding to OD and area evaluations, respectively) and good to excellent for the device (the ICC values were 0.88 [95% CI: 0.83–0.92] in area, 0.85 [95% CI: 0.79–0.90] in MD, and 0.85 [95% CI: 0.78–0.90] in OD). The consistency of Nexkin DSPT® readings appeared to be greater than those of the manual procedure. Reading variations in area (Figure 2) for Nexkin DSPT® (2.02 mm²; SD = 3.42) were lower than those of the manual procedure (4.94 mm²; SD = 4.14) ($p < .001$). Similar results were obtained for MD and OD of wheals. Additional results are included in Appendix S1.

Overall, the agreement between the device and manual procedure was moderate. Although no gold standard method exists,⁵ the automatic measurement system of the device seems to be more appropriate to yield less variable measurements than the manual procedure, as the results from the device are regardless of the individual who performs SPT and/or the thickness of the pen used to outline the wheals.⁶ The discussion was expanded in Appendix S1.

The results suggest a higher reliability of the electro-medical device Nexkin DSPT® for the measurement of wheal area in SPT, compared to the manual procedure. This device has potential for improving the uniformity of the reading phase of the SPT and,

María de la Paz Morales-Palacios and Jorge M. Núñez-Córdoba contributed equally.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2022 The Authors. *Allergy* published by European Academy of Allergy and Clinical Immunology and John Wiley & Sons Ltd.

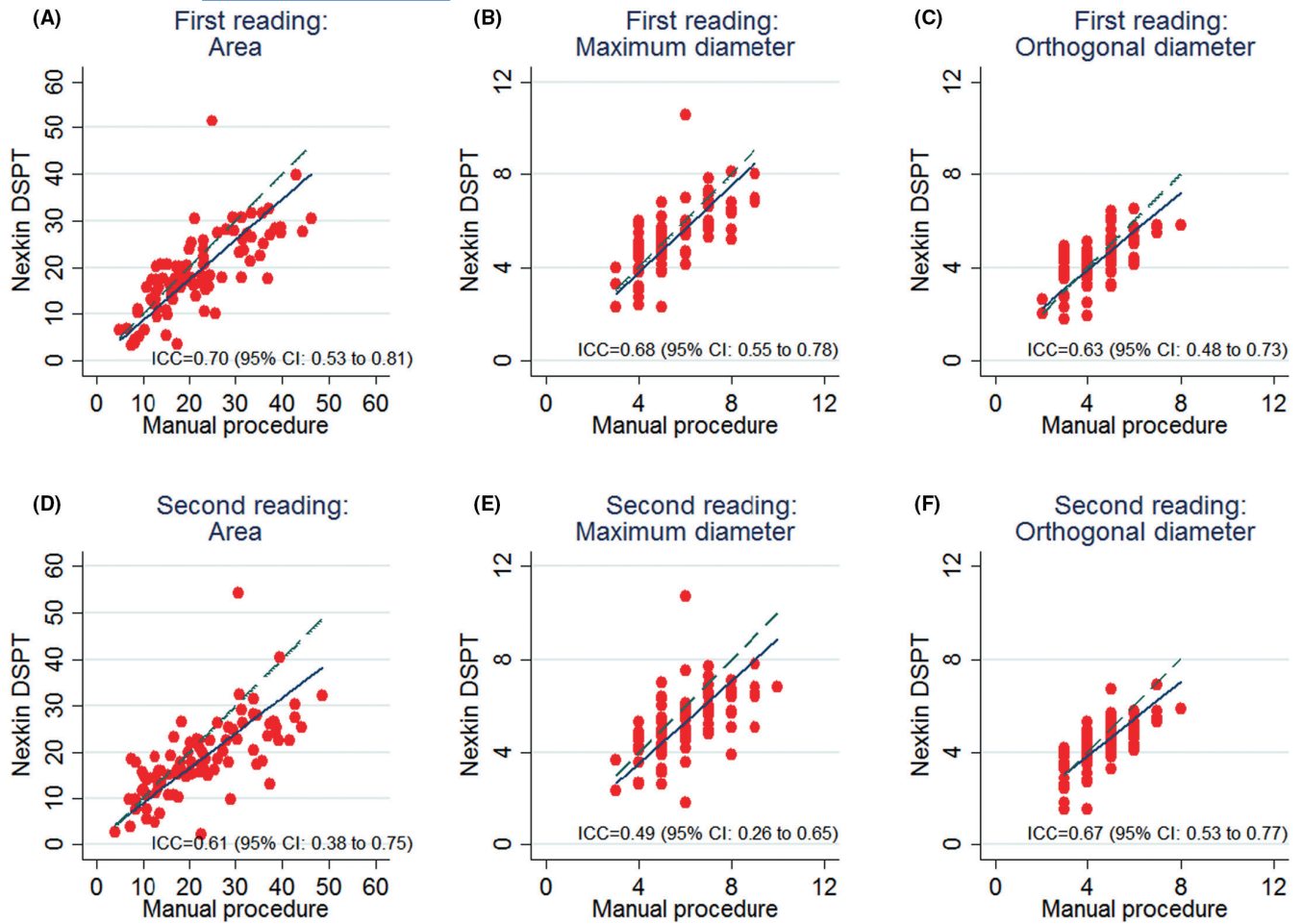


FIGURE 1 Agreement in wheal size between manual measurement procedure and Nexkin DSPT® for first and second readings. 95% CI, 95% confidence interval; ICC, Intraclass correlation coefficient. Dashed lines represent perfect agreement and solid lines indicate reduced major axis (RMA) linear regression

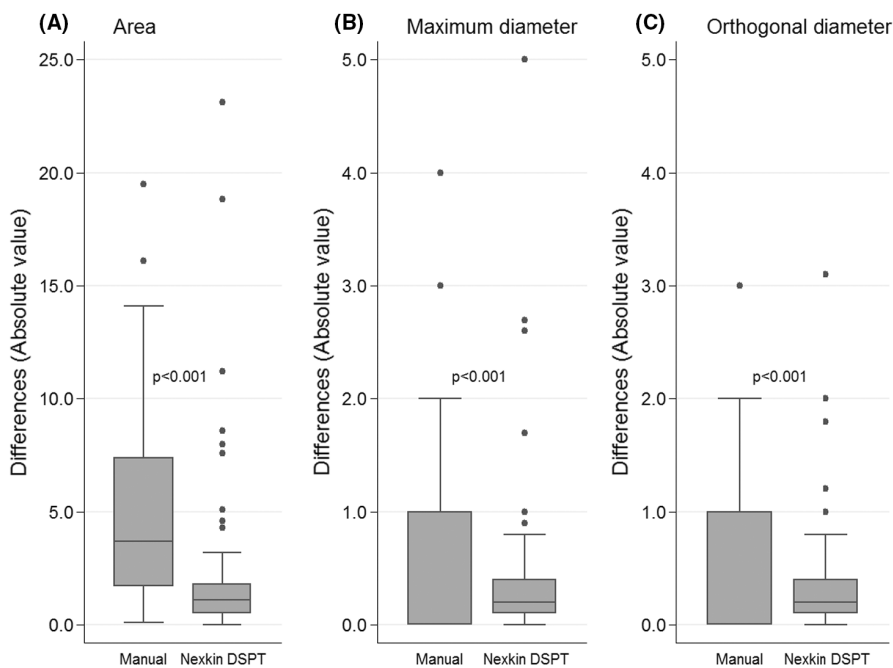


FIGURE 2 Comparisons between histamine wheal size reading variations of manual procedure and Nexkin DSPT®

therefore, it may favour standardization, upgrade, and innovation of the current SPT technique.

ACKNOWLEDGEMENTS

We wish to thank Mr. Gustavo Pego, from Innovation Factory of the University of Navarra, for promoting this project.

KEYWORDS

allergy, automated measurement, clinical trial, diagnosis, prick test

FUNDING INFORMATION

The study was supported by Nexkin Medical.

CONFLICT OF INTEREST

GG is a member of the Nexkin Medical advisory board and patent's co-author: Measuring Wheals and Detecting Allergies. OM and ET are Nexkin Medical employees and shareholders. The remaining authors have no conflicts of interests.

María de la Paz Morales-Palacios¹ 

Jorge M. Núñez-Córdoba² 

Eduardo Tejero³

Óscar Matellanes³

Paola Leonor Quan¹ 

Álvaro Carvallo¹

Sergio Sánchez-Fernández¹

Maite Urtasun¹

Carla Larrea¹

María Teresa Íñiguez¹

Rosa Giménez¹

Maria José Goikoetxea^{1,4}

Carmen M. D'Amelio^{1,4}

Marta Ferrer^{1,4} 

Gabriel Gastaminza^{1,4} 

¹Department of Allergy and Clinical Immunology, Clínica Universidad de Navarra, Pamplona, Spain

²Central Clinical Trials Unit, Research Support Service, Clínica Universidad de Navarra, Pamplona, Spain

³Nexkin Medical, Donostia-San Sebastián, Spain


⁴Spanish Research Network on Allergy RD 1600060031 (ARADyAL: Red Nacional de Alergia -Asma, Reacciones Adversas y Alérgicas) of the Carlos III Health Institute, Madrid, Spain

Correspondence

Gabriel Gastaminza, Clínica Universidad de Navarra, Av. Pio XII, 36, Pamplona 31008, Spain.
Email: gastaminza@unav.es

ORCID

María de la Paz Morales-Palacios  <https://orcid.org/0000-0002-3059-6234>

Jorge M. Núñez-Córdoba  <https://orcid.org/0000-0002-8109-9529>

Paola Leonor Quan  <https://orcid.org/0000-0003-1542-1919>

Marta Ferrer  <https://orcid.org/0000-0001-8495-1302>

Gabriel Gastaminza  <https://orcid.org/0000-0001-6325-3847>

REFERENCES

1. Klimek L, Hoffmann HJ, Kalpaklioglu AF, et al. In-vivo diagnostic test allergens in Europe: a call to action and proposal for recovery plan—An EAACI position paper. *Allergy*. 2020;75(9):2161-2169.
2. Ansotegui IJ, Melioli G, Canonica GW, et al. IgE allergy diagnostics and other relevant tests in allergy, a World Allergy Organization position paper. *World Allergy Organ J*. 2020;13(2):100080.
3. Justo X, Díaz I, Gil JJ, Gastaminza G. Prick test: evolution towards automated reading. *Allergy*. 2016;71:1095-1102.
4. Justo X, Diaz I, Gil JJ, Gastaminza G. Medical device for automated prick test reading. *IEEE J Biomed Health Inform*. 2018;22(3):895-903.
5. Buyuktiryaki B, Sahiner UM, Karabulut E, Cavkaytar O, Tuncer A, Sekerel BE. Optimizing the use of a skin prick test device on children. *Int Arch Allergy Immunol*. 2013;162(1):65-70.
6. Portnoy J. Diagnostic testing for allergies. *Ann Allergy Asthma Immunol*. 2006;96:3-4.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

DOI: 10.1111/all.15476

Outcomes of COVID-19 vaccination in 323 patients with clonal and non-clonal mast cell activation disorders

To the Editor,
SARS-CoV-2 vaccines are proven to be safe and effective.¹ The vaccines are overall well tolerated although hypersensitivity reactions

have been reported, which are more frequent in females with atopy and those with a history of anaphylaxis.² The reports of anaphylaxis are of concern for patients with mast cell activation