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LETTER

Assessment of the Severity of Atopic Dermatitis Using Atomic Force Microscopy Analysis of Skin Tape Strips

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To the Editor,

Atopic dermatitis (AD) is a common eczematous skin disorder driven by immune responses and skin barrier defects [1]. Atomic force microscopy (AFM) unravels structural changes in the skin barrier [2]. Villus-like protrusions of a few hundred nanometers, termed circular nanosize objects (CNOs), are observed on the basal side of corneocytes in AD patients [3]. This study evaluated correlations between CNO abundance and AD severity using the Effective Corneocyte Topographical Index (ECTI), which combines the AFM, deep learning, and spatial analysis algorithms to precisely calculate CNO density by dividing the number of detected CNOs by the effective skin area [4].

A total of 120 individuals were recruited from National Taiwan University Hospital in Taipei, Taiwan (June 2022–September 2022) and Bispebjerg Hospital in Copenhagen, Denmark (September 2022–May 2023). Participants were divided into four groups (healthy control [HC], G1, G2, and G3) based on AD history and Eczema Area and Severity Index (EASI) (Table S1). No participants had other skin diseases, active infections, or had applied topical corticosteroids within 3 days prior to sampling. Skin samples were collected using tape strips, and the ECTI and natural moisturizing factor (NMF) data were obtained (Appendix S1). This study was approved by the National Taiwan University Hospital Research Ethics Committee (202204089RIND) and the Danish Research Ethics Committees (2207232). All patients provided written informed consent.

We found that the ECTI increased with AD severity and positively correlated with the EASI (Figure S1A). Figure 1A shows representative AFM images from each group, along with their ECTI values. The ECTI was significantly higher in lesional skin than in non-lesional skin of AD patients, which was subsequently higher than in HC (Figure 1B), highlighting its sensitivity to subclinical skin barrier changes. While this trend was consistent across both Taiwanese and Danish cohorts, mean ECTI values were significantly higher for Taiwanese in the HC and non-lesional AD groups (Figure 1C). The ECTI increases with rising AD severity, even in non-lesional skin (Figures 1D and S1B).

NMF levels exhibited an inverse trend compared to the ECTI (Figure S1C) and were significantly higher in healthy skin than in lesional and non-lesional AD skin (Figure 1E). Unlike the ECTI, only the NMF of the non-lesional AD skin was significantly different between Taiwanese and Danish individuals (Figure 1F). The NMF levels of the three AD severity groups and the HC group could not be significantly differentiated, but they revealed a decreasing trend with increasing AD severity (Figure 1G).

Edwin En-Te Hwu and Chia-Yu Chu contributed equally to this study.

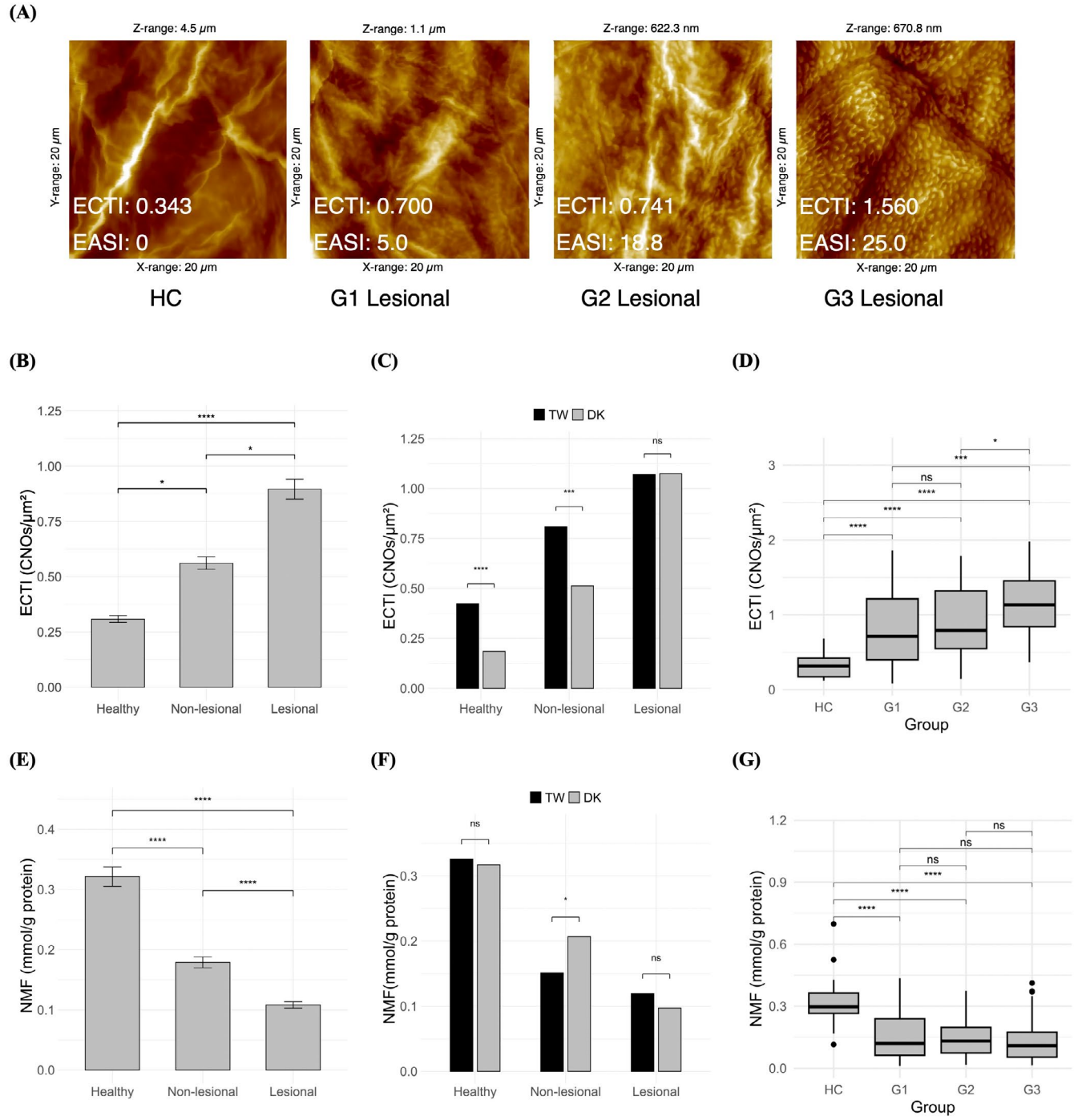

FIGURE 1 | Corneocyte surface topography and measurements of ECTI and NMF in atopic dermatitis patients and healthy controls. (A) Representative AFM images of corneocyte surface topography and ECTI in HC, G1, G2, and G3. (B–D) ECTI comparisons in lesional vs. non-lesional versus HC skin, between Taiwanese and Danish cohorts, and across AD severity groups relative to HC. (E–G) Corresponding NMF comparisons in the same categories as panels B–D. Statistical significance: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, and ****$p < 0.0001$, G1–G3, AD severity groups by EASI score; HC, healthy controls; ns, Not significant.

We found no correlation between the ECTI and age (Figure S1D). While aging affects skin textures, studies report inconsistent findings on the relationship between corneocyte topography and age, suggesting the distinct mechanism in skin nanoscale changes [5, 6].

This study highlights the positive correlations between CNO density, captured by AFM using the novel ECTI approach, and clinical severity of AD both generally (assessed by the EASI) and locally (represented by the Target Lesion Severity Score, Figure S1E). Mechanisms underlying the formation and function of CNOs are unclear but likely involve impaired corneocyte maturation due to filaggrin (FLG) protein deficiency, disrupted connection between intermediate keratin filaments and corneodesmosomes, and alterations of lipids and proteins in the cornified envelope [3].

This study's limitations include the lack of FLG mutation analysis and the differing environmental conditions during tape sampling between Taiwan and Denmark. However, by pairing the ECTI with NMF levels, this study provided a more comprehensive assessment of skin barrier function, allowing for correlation between structural changes in corneocytes and biochemical parameters of stratum corneum hydration.

We investigated ECTI as a rapid, non-invasive, and reproducible approach to evaluating AD severity, with clinical implications for objective disease monitoring of treatment responses. Longitudinal analysis of the ECTI may enable early detection of subclinical changes in AD.

Author Contributions

C.-W.D. designed the sample collection protocols and compiled the dataset; J.-H.W. developed the source code, annotated the dataset, and fine-tuned the deep learning models with support from J.P. and A.D.; C.-W.D., C.-Y.C., and M.O.C. collected the samples; I.J. did the analysis of the natural moisturizing factors; I.J., M.O.C., and S.K. provided technical feedback and interpretation of results throughout the development phase; C.-Y.C. and E.E.-T.H. contributed to the critical revision of the manuscript; C.-Y.C., J.P.T., and E.E.-T.H. conceptualized and designed the project. All authors contributed to and approved the final manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data supporting the findings of this study are publicly available. Access to the dataset may be requested from the corresponding authors.

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References

1. M. Boguniewicz and D. Y. Leung, "Atopic Dermatitis: A Disease of Altered Skin Barrier and Immune Dysregulation," *Immunological Reviews* 242, no. 1 (2011): 233–246.

2. J. Pereda, C. Milde Khatib, S. Kezic, et al., "A Review of Atomic-Force Microscopy in Skin Barrier Function Assessment," *Journal of Investigative Dermatology* 144, no. 10 (2024): 2136–2144.

3. C. Riethmuller, M. A. McAleer, S. A. Koppes, et al., "Filaggrin Breakdown Products Determine Corneocyte Conformation in Patients With Atopic Dermatitis," *Journal of Allergy and Clinical Immunology* 136, no. 6 (2015): 1573–1580.e2.

4. J. H. Wang, J. Pereda, C. W. Du, et al., "Stratum Corneum Nanotexture Feature Detection Using Deep Learning and Spatial Analysis: A Noninvasive Tool for Skin Barrier Assessment," *GigaScience* 13 (2024): giae095.

5. J. Franz, M. Beutel, K. Gevers, et al., "Nanoscale Alterations of Corneocytes Indicate Skin Disease," *Skin Research and Technology* 22, no. 2 (2016): 174–180.

6. K. A. Engebretsen, S. Kezic, C. Riethmuller, et al., "Changes in Filaggrin Degradation Products and Corneocyte Surface Texture by Season," *British Journal of Dermatology* 178, no. 5 (2018): 1143–1150.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Appendix S1:** all70170-sup-0001-AppendixS1.docx. **Data S1:** all70170-sup-0002-Supinfo.docx.