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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No software or automation were used for data collection. All data were collected manually from patient records and entered a pre-specified form by study investigators. Also, ratings from each reader were extracted in a pre-specified form for further analyses. That information is available in "Methods" section ("Data source - Patient population", "Participant selection - Web-based study interface - Procedure for lesion evaluation" , "Assessment of ratings")
Data analysis	Regarding data analysis, R code for the DMFS calculation is available under MIT license on Zenodo at https://doi.org/10.5281/zenodo.17418482 . The statistical analysis plan is reported in detail in "Statistical Analysis Section". "Continuous variables were expressed as mean ± standard deviation, and categorical variables were summarized using frequencies. Interrater agreement was evaluated with Krippendorff's alpha coefficient, interpreted according to the Landis and Koch classification. Median follow-up time was estimated via the reverse Kaplan-Meier method. Group comparisons for continuous variables (Breslow thickness and age) used the Mann-Whitney U test. Associations between dermatoscopic features and melanoma metastasis were analyzed using χ^2 tests. We employed univariate and multivariable logistic regression models to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for metastasis risk and to develop predictive models based on dermatoscopic, clinical, or histologic predictors. Backward elimination was used for automated variable selection during model construction. To further assess the predictive utility of dermatoscopy, we conducted Cox proportional hazards regression analyses exclusively in early-stage melanomas (AJCC stage IB–II), excluding cases with metastatic events at diagnosis. Study endpoints included recurrence-free survival (RFS), defined as the time from diagnosis to first metastasis, and distant metastasis-free survival (DMFS), defined as the interval from diagnosis to distant metastatic spread. Hazard ratios (HRs) and survival probabilities were calculated, with model performance quantified using the area under the receiver operating characteristic curve (AUC). For robustness, logistic and Cox regression analyses were performed using a dataset split into training and test sets, stratified by TNM stage, age, and sex. A 5-fold cross-validation approach was applied to the training set to evaluate the diagnostic accuracy of the three models,

followed by independent validation in the test set. We used DeLong's test to compare AUC values across models. All statistical tests were two-sided, and analyses were conducted using R packages (R version 4.5.1) and IBM SPSS Statistics (v29.0)."

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Raw clinical data and dermatoscopic images are not publicly available due to lack of permission from data sources to have those data distributed to third parties. Access can be obtained for academic and research purposes by submitting a request to the corresponding author (A.L.), by email at alallas@auth.gr. Requests should include the applicant's name, contact details, affiliation and the intended use of the data. The corresponding author is responsible to contact collaborating centers and initiate the data-sharing process. Applications will be evaluated based on institutional policies. Clinical data and digitally annotated dermatoscopic image will only be shared following necessary institutional approvals. For centers that cannot provide consent for data sharing, specific reasons will be communicated to the applicants. An initial response from the corresponding author is anticipated within one month of request submission and the final acceptance or not from collaborating centers will be provided within the next three months. All remaining data supporting this work are available in the main article, supplementary information or Source data File.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Patient sex (male/female) was abstracted from medical records. Human reader sex was self-reported (Methods section, "Data Source-Patient population" and "Participants selection – Web-based study interface-Procedure for lesion evaluation" subheadings).Regarding patient sex (male/female), predictive models of metastasis were adjusted for clinical factors, such as age, gender, anatomic location, according to reviewer's suggestion. Sex of human rates was not analysed further in our study.
Reporting on race, ethnicity, or other socially relevant groupings	This was a retrospective observational studies focusing on the role on dermatoscopy on melanoma metastasis. No data was collected regarding race or ethnicity of patients with melanoma. Also, ethnicity of each reader participated into evaluation of dermatoscopic images was recorded, but it was not further analyzed as it was not relevant to primary and secondary outcomes.
Population characteristics	There is a detailed description of patient population included in the study in methods section. More precise, "Ten skin cancer centers worldwide participated in the study, including seven in Europe, one in South America, one in Asia and one in the United States. Clinical and histopathologic data from patients diagnosed with cutaneous melanoma stage IB and above between 2013 and 2018, along with dermatoscopic images of the primary tumor, and documented follow-up were collected from collaborating institutions. The median time to metastasis in the literature ranges from 25 to 30 months after diagnosis. Therefore, we considered a lesion as non-metastatic if no metastasis was detected after a 36-month follow-up period. Exclusion criteria were missing clinicopathological data, lack of dermatoscopic image of the primary lesion, and an inadequate follow-up period. "
Recruitment	Regarding recruitment of patients in this retrospective study, all patients with melanoma who were followed up in participating centers and aligned with inclusion criteria were included. Regarding human readers recruitment, there is a detailed description in methods section. More precise, "Thirty raters were invited via e-mail to annotate pseudonymized cases on a web-based platform using structured questions. The goal was to recruit at least two readers from each center, each with a minimum of 5 years of experience in dermatoscopy. Details on the collaborators and number of readers per center are available in Supplementary Table 20."
Ethics oversight	Ethics committee approval was obtained by the School of Medicine of Aristotle University of Thessaloniki. The study was retrospective, had no impact on patient management, and used fully anonymized datasets and de-identified dermatoscopic images.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The sample size estimation was included in the study protocol submitted and approved by the Ethics Committee of Aristotle University of Thessaloniki. Based on previous observational studies, we assumed that approximately 30% would progress to stage III or stage IV (regional or distant metastasis). Using an estimated rate of metastasis of 25%, assuming an Odds Ratio (OR) of 2.0 to detect meaningful associations and setting power 0.8 and two-sided alpha level 0.05, we calculated a sample size of 476 patients would be required. To maximize statistical power, we included all eligible cases from participating centers that met the inclusion criteria, resulting in final study population of 524 patients.
Data exclusions	inclusion and exclusion criteria were pre-specified in the study protocol before data collection and were applied uniformly across centers. Patients were excluded if they lacked dermatoscopic images of the primary tumor, essential clinical and histopathological variables needed for models development and adequate follow-up to ascertain metastasis outcomes. The above criteria are detailed in Methods section ("Data source - Patient population"). These exclusions were chosen to minimize information bias and to ensure that predictors and outcomes were measured consistently.
Replication	To assess robustness and reproducibility of our results, we performed a stratified train/test split of the dataset (stratified by TNM, age,sex) and 5-fold cross validation within the training set. Details of the internal validation procedures are provided in Methods ("Outcomes" - "Statistical analysis plan"). Models' performance for metastasis prediction, recurrence-free survival and distant metastasis-free survival were comparable in training and test sets. Also, we adjusted models for clinical factors (age, sex, anatomic location) and additionally for histopathologic subtype, as suggested and the results remained unaltered. In addition, we conducted several sensitivity analyses (by anatomic location, excluding patients with acral or subungual melanomas or by metastatic status at diagnosis) and subgroup analyses based on clinically relevant Breslow thickness thresholds, all yielding consistent conclusions. All analyses are reproducible with the materials provided: Source data for image generation, R code for DMFS calculation. We did not encounter findings that failed to replicate internally.
Randomization	This was a retrospective observational study and randomization was not applicable to study design.
Blinding	This was a retrospective observational study and blinding was not applicable to study design. However, readers who evaluated the dermatoscopic images of primary tumors were blinded to the outcomes (metastasis or not metastasis). This is stated in "Methods" section, subheading "Criteria for lesion evaluation" with the statement "Dermatoscopic images were independently evaluated by human readers in a blinded manner, based on pre-specified criteria and according to established terminology".

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	This was a retrospective observational study and there is not any clinical trial protocol registration.
Study protocol	A study protocol was submitted and approved by the Ethics Committee of Aristotle University of Thessaloniki (protocol number 29945/20). This was a retrospective, observational study conducted according to REMARK guidelines (provided in Supplementary Information). The study design, inclusion criteria and statistical analysis plan are detailed in the Methods section of the manuscript.
Data collection	Clinical and histopathological data from patients with melanoma were retrospectively collected from medical records by investigators at ten participating skin cancer centers across the globe, using a standardized pre-specified data collection form. Data collection was conducted by the first and corresponding author after contacting each center separately. Dermatoscopic images of primary melanomas were de-identified and uploaded to a web-based platform, where 30 dermatologists, with experience in dermatoscopy, independently evaluated them according to pre-specified dermatoscopic criteria between 21 October 2023 and 10 March 2024.
Outcomes	An analytic presentation of the primary and secondary outcomes of the study are provided in Methods section, subheading

"Outcomes". More precise, "The primary outcome of the study was to investigate the association between dermatoscopic features of primary melanoma and metastasis (n=524 patients). Metastasis was defined as any metastatic event occurring either at initial diagnosis or during subsequent follow-up, encompassing regional disease (i.e., in-transit and satellite metastases, sentinel lymph node biopsy positivity, or completion lymph node dissection positivity) and distant metastatic spread.

Secondary outcomes included developing a predictive model for metastasis based on dermatoscopy (Model 1) and comparing its diagnostic accuracy with a model incorporating established melanoma prognostic factors (i.e., Breslow thickness and ulceration) (Model 2), as well as a combined model integrating both dermatoscopic and histopathologic predictors (Model 3). An additional secondary outcome was the comparison of the accuracy of all three models in predicting recurrence-free survival (RFS) and distant metastasis-free survival (DMFS) in early-stage tumors at diagnosis (n=381 patients)."

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.