

This is the peer reviewed version of the following article:

Dermoscopy of cutaneous squamous cell carcinoma by anatomical location and risk stratification: a retrospective cross-sectional study / Spadafora, Marco; Cavicchi, Martina; Lippolis, Nicola; Piana, Simonetta; Bertoni, Laura; Kaleci, Shaniko; Chester, Johanna; Paganelli, Alessia; Pellacani, Giovanni; Longo, Caterina. - In: JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY. - ISSN 0190-9622. - (2026), pp. 1-10. [10.1016/j.jaad.2026.04.1935]

Terms of use:

The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

16/05/2026 23:44

(Article begins on next page)

Journal Pre-proof

Dermoscopy of cutaneous squamous cell carcinoma by anatomical location and risk stratification: a retrospective cross-sectional study

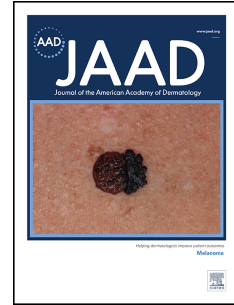
Marco Spadafora, MD, PhD, Martina Cavicchi, MD, Nicola Lippolis, MD, Simonetta Piana, MD, Laura Bertoni, Shaniko Kaleci, PhD, Johanna Chester, BA/BBS, Alessia Paganelli, MD, PhD, Giovanni Pellacani, MD, Caterina Longo, MD, PhD

PII: S0190-9622(26)02530-2

DOI: <https://doi.org/10.1016/j.jaad.2026.04.1935>

Reference: YMJD 21189

To appear in: *Journal of the American Academy of Dermatology*



Please cite this article as: Spadafora M, Cavicchi M, Lippolis N, Piana S, Bertoni L, Kaleci S, Chester J, Paganelli A, Pellacani G, Longo C, Dermoscopy of cutaneous squamous cell carcinoma by anatomical location and risk stratification: a retrospective cross-sectional study, *Journal of the American Academy of Dermatology* (2026), doi: <https://doi.org/10.1016/j.jaad.2026.04.1935>.

This is a PDF of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability. This version will undergo additional copyediting, typesetting and review before it is published in its final form. As such, this version is no longer the Accepted Manuscript, but it is not yet the definitive Version of Record; we are providing this early version to give early visibility of the article. Please note that Elsevier's sharing policy for the Published Journal Article applies to this version, see: <https://www.elsevier.com/about/policies-and-standards/sharing#4-published-journal-article>. Please also note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2026 Published by Elsevier Inc. on behalf of the American Academy of Dermatology, Inc.

Article type: *Brief report*

Title: Dermoscopy of cutaneous squamous cell carcinoma by anatomical location and risk stratification: a retrospective cross-sectional study

Marco Spadafora, MD, PhD¹, Martina Cavicchi, MD², Nicola Lippolis, MD,³ Simonetta Piana, MD,⁴ Laura Bertoni¹, Shaniko Kaleci, PhD,¹ Johanna Chester, BA/BBS,¹ Alessia Paganelli, MD, PhD,⁵ Giovanni Pellacani, MD,⁶ Caterina Longo, MD, PhD^{1,2}

Institutional affiliations:

1. Department of Surgery, Medicine, Dental Medicine and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy
2. Department of Dermatology, Azienda Ospedaliero-Universitaria Policlinico di Modena, Italy
3. Azienda Unità Sanitaria Locale – IRCCS di Reggio Emilia, Skin Cancer Center, Reggio Emilia, Italy
4. Pathology Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy
5. Istituto Dermopatico dell'Immacolata - Istituto di Ricovero e Cura a carattere Scientifico (IDI-IRCCS), Rome, Italy
6. Dermatology Clinic, Department of Clinical Internal, Anesthesiological and Cardiovascular Sciences, Sapienza University of Rome, Rome, Italy

E-mail addresses:

marco.spadafora@unimore.it, martycavicchi@gmail.com, n.lippolis2@gmail.com,
simonetta.piana@ausl.re.it, laura.bertoni@unimore.it, shaniko.kaleci@gmail.com,

caterina.longo@unimore.it

Corresponding Author:

Prof. Caterina Longo, MD, PhD

Department of Surgery, Medicine, Dental Medicine and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy

Email: caterina.longo@unimore.it

ORCID: <https://orcid.org/0000-0002-8218-3896>

Funding sources: Dr Marco Spadafora was supported by Italian Ministry of University and Research (MUR), through the PRIN 2022 Project “Cutaneous squamous cell carcinoma: stratifying high risk tumours with novel technologies” project code 2022MZEEZB (CUPE53D23013260006) funded by National Recovery and Resilience Plan (PNRR), Italy, Mission 04 Component 2 Investment 1.1 – NextGenerationEU.

Conflicts of Interest: None declared.

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement: All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The patients in this manuscript have given written informed consent to publication of their case details. This study was approved by the Institutional Review Board of Azienda Unità Sanitaria Locale – IRCCS di Reggio Emilia, Italy (CE: CE: 875/2020/OSS/IRCCSRE).

Author Contributions: Conceptualization: CL; Methodology: CL, MS, SK; Investigation: MS, MC, NL, SP, AP, LB; Data curation: MS; Formal analysis: SP, SK; Writing – original draft: MS; Writing – review and editing: MS, JC; Supervision: CL, GP

Manuscript word count: 500

Figure count: 0

Table count: 2

Supplemental material: <https://data.mendeley.com/datasets/c9chrhr7vb/1>

Keywords: cutaneous squamous cell carcinoma, risk stratification, NCCN, very-high risk, high-risk, diagnosis, dermoscopy, anatomical location

Journal Pre-proof

1 **TEXT**

2 Cutaneous squamous cell carcinoma (cSCC) is a common skin cancer; prognosis is usually
3 favorable, yet a clinically relevant subset carries a risk of recurrence and metastasis.^{1,2} With the
4 2022 NCCN update adding the “very-high risk” category, dermoscopic correlates across anatomical
5 sites and risk categories warrant better characterization.³ We evaluated dermoscopic features of
6 invasive cSCC (iSCCs) by macro-anatomical location and NCCN risk category and explored
7 dermoscopic predictors of very-high risk tumors defined by histopathological poor differentiation.

8 We retrospectively reviewed histopathologically confirmed iSCCs with dermoscopic images
9 collected at an Italian Skin Cancer Center (2011-2021). Nail and genital tumors were excluded.
10 Lesions were grouped into macro-areas (head/neck, trunk, upper/lower limbs, acral sites) and
11 classified as low-, high-, or very-high risk according to NCCN criteria³. Two dermatologists
12 assessed dermoscopic criteria while blinded to clinical data, risk group, and histopathology^{4,5}.
13 Group comparisons used univariate testing; logistic regression to identify predictors of poor
14 differentiation was performed for head/neck only due to cohort distribution. No formal correction
15 for multiple testing was applied, to avoid an excessive increase in type II error.

16 We analyzed 768 iSCCs; most occurred on the head/neck (79.9%) and most patients were male
17 (76.8%). Differentiation grade was available for 668 tumors; poorly differentiated cSCCs were
18 often located on lower limbs (71.4%) and acral sites (52.0%) ($p<0.001$). Dermoscopy showed site-
19 related differences: small-caliber vessels predominated on upper limbs (73.8%) and acral sites
20 (75.9%); diffuse (whole-lesion) vascularity was common on the trunk (70.4%) and lower limbs
21 (62.5%), whereas a peripheral distribution prevailed on acral sites (73.4%) and head/neck (51.9%)
22 ($p<0.001$). Dotted-glomerular vessels were frequent overall (65.6%, $p<0.001$); conversely,
23 arborizing vessels were more common on trunk (38.6%) and head/neck (30.8%) ($p<0.001$).
24 Ulceration occurred in 61.0%, particularly on head/neck and limbs ($p<0.001$). Pink structureless

25 areas were common (78.4%) without anatomical differences; white circles were uncommon but
26 more frequent on head/neck (13.9%). Yellow crust was typical of acral sites, head/neck, and lower
27 limbs (75.5%, 65.2%, and 63.5%, respectively; $p=0.038$).

28 By NCCN risk category, 8.5% were low-risk, 79.4% high-risk, and 12.2% very-high risk; age
29 increased with risk severity ($p<0.001$) (**eTable**). Low-risk tumors often showed small-caliber,
30 dotted-glomerular or hairpin vessels and white scale, whereas higher-risk tumors more often
31 showed linear irregular or arborizing vessels and ulceration ($p<0.001$) (**Table 1**). On head/neck,
32 independent predictors of poor differentiation were age (OR 1.03 per year; $p=0.044$), ulceration
33 (OR 2.27; $p=0.002$), and yellow crust (OR 1.70; $p=0.039$) (**Table 2, eFigure**), while peripheral
34 vessel distribution, dotted-glomerular vessels, and white circles were protective (**eFigure 2**).

35 In conclusion, dermoscopic patterns in iSCC vary by anatomical location and NCCN risk category.
36 Acral lesions showed the most distinctive profile (small peripheral vessels and frequent central
37 keratin or yellow crust, but rare ulceration). Poor differentiation (very high-risk tumor) was
38 independently associated with older age, ulceration, and yellow crust. Notably, yellow crust may
39 reflect purulent material/dried exudate from local contamination/secondary infection rather than
40 keratinization (white scale), potentially contributing to higher prevalence in head/neck, lower-limb,
41 and acral sites. Dermoscopy may support earlier risk upgrading while histology is pending,
42 although the retrospective design warrant validation.

1. Paganelli A, Zaffonato M, Donati B, et al. Molecular and Histopathological Characterization of Metastatic Cutaneous Squamous Cell Carcinomas: A Case-Control Study. *Cancers (Basel)*. 2024;16(12):2233. doi:10.3390/cancers16122233
2. Schmults CD, Karia PS, Carter JB, Han J, Qureshi AA. Factors predictive of recurrence and death from cutaneous squamous cell carcinoma: a 10-year, single-institution cohort study. *JAMA Dermatol*. 2013;149(5):541-547. doi:10.1001/jamadermatol.2013.2139
3. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology: Squamous Cell Skin Cancer*. Accessed January 3, 2026. https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf
4. Lallas A, Pyne J, Kyrgidis A, et al. The clinical and dermoscopic features of invasive cutaneous squamous cell carcinoma depend on the histopathological grade of differentiation. *Br J Dermatol*. 2015;172(5):1308-1315. doi:10.1111/bjd.13510
5. Rosendahl C, Cameron A, Argenziano G, Zalaudek I, Tschandl P, Kittler H. Dermoscopy of squamous cell carcinoma and keratoacanthoma. *Arch Dermatol*. 2012;148(12):1386-1392. doi:10.1001/archdermatol.2012.2974

Table 1. Descriptive characteristics and comparisons among different risk groups

Variable	Total, n=1536	Low risk, n=130 (8.5)	High risk, n=1220 (79.4)	Very High Risk, n=186 (12.2)	p-value
Age*, mean \pm SD (range)	80.4 \pm 10.0 (37-102)	76.3 \pm 12.1 (37-95)	80.6 \pm 9.8 (39-102)	81.9 \pm 8.9 (41-96)	<0.001
Sex (male)	1180 (76.8)	88 (67.7)	948 (77.7)	144 (77.4)	0.036
Caliber (vessels)					
small	708 (51.9)	82 (70.1)	553 (51.2)	73 (43.2)	<0.001
large	182 (13.3)	11 (9.4)	148 (13.7)	23 (13.6)	
both	475 (34.8)	24 (20.5)	378 (35.0)	73 (43.2)	
Distribution (vessels)					
whole lesions	612 (44.8)	64 (54.7)	453 (42.0)	95 (56.2)	0.002
center	36 (2.6)	1 (0.8)	31 (2.9)	4 (2.4)	
periphery	694 (50.8)	52 (44.4)	576 (53.4)	66 (39.0)	
cluster	23 (1.7)	0 (0.0)	19 (1.8)	4 (2.4)	
Dotted-glomerular	895 (65.6)	90 (76.9)	706 (65.4)	99 (58.6)	0.006
Arborizing vessels	384 (28.1)	15 (12.8)	315 (29.2)	54 (31.9)	<0.001
Hairpin vessels	368 (27.0)	34 (29.1)	305 (28.3)	29 (17.2)	0.009
Linear irregular vessels	1170 (85.7)	85 (72.6)	927 (85.9)	158 (93.5)	<0.001
Ulceration	936 (61.0)	56 (43.1)	744 (61.0)	136 (73.1)	<0.001
Pinkish structureless area	1204 (78.4)	91 (70.0)	982 (80.5)	131 (70.4)	<0.001
White halo	799 (52.1)	70 (53.8)	638 (52.3)	91 (49.2)	0.665
White circles	185 (112.0)	7 (5.4)	163 (13.4)	15 (8.1)	0.006
White scales	866 (56.5)	88 (67.7)	688 (56.5)	90 (48.4)	0.003
Central keratin distribution	661 (43.1)	53 (40.8)	539 (44.2)	69 (37.1)	0.162
Yellow scales	997 (64.9)	72 (55.4)	798 (65.5)	127 (58.3)	0.043

Table 2 - Multivariate model for histopathology grading of differentiation in SCC of the head and neck (well-moderate vs poor differentiated/very high risk)

	Multivariate model		
	OR	95%CI	P value
Demographic criteria			
Age at diagnosis, mean yrs \pm SD(range)	1.03	1.00-1.05	.04
Dermoscopy criteria			
Vessels distribution			
Whole lesion	ref.		
Center	0.30	0.6-1.49	.142
Periphery	0.38	0.23-0.62	.000
Cluster	1.55	0.22-9.18	0.79
Dotted-glomerular vessels	0.43	0.26-0.70	.001
Ulceration	2.27	1.33-3.84	.002
White circles	0.38	0.17-0.86	.02
Yellow crust	1.70	1.03-2.81	.039

Abbreviations: OR, odds ratio; SD, standard deviation; CI, confidence interval

Journal Pre-proof