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Nipple and areola lesions: Dermoscopy and reflectance confocal microscopy features



To the Editor: Only case reports have analyzed the dermoscopic and reflectance confocal microscopy (RCM) features of the lesions of nipple and areola complex (NAC).¹⁻³ We retrospectively evaluated the clinical, dermoscopic, and RCM features of 131 consecutive NAC lesions diagnosed at 13 University Centers (Tables I and II). The final diagnosis was based on histopathology or on clinical follow-up for ≥ 1 year to confirm benignity. Three experts in noninvasive skin imaging (EC, MA, and SG) independently evaluated dermoscopic and RCM criteria blinded from the diagnosis. Criteria were considered present when ≥ 2 experts agreed (Table II). A 7-point checklist⁴ and Pellacani criteria⁵ have been developed for melanocytic lesions but were applied to all lesions because in the NAC it is not always easy to clinically establish if lesions are melanocytic or not. Considering Paget disease (PD) and eczema, we found a statistically significant difference for both for the presence of spongiosis (Fisher exact test, $P = .017$) and dark Paget cells ($P = .038$) under RCM but no difference for the

presence of dotted ($P = .587$) and linear vessels ($P = 1.000$) and milky-red areas ($P = .052$) under dermoscopy.

Diagnostic accuracy of the 3 types of examination was calculated on the agreement of ≥ 2 of 3 investigators for 79 lesions with clinical, dermoscopic, and RCM images. Sensitivity and 95% confidence intervals (95% CIs) for malignancy of the clinical, dermoscopic, and RCM examination were 83% (73-90%), 67% (55-77%), and 83% (73-90%) and specificity (95% CIs) were 90% (80-95%), 97% (90-99%), and 94% (86-98%), respectively. Specificity of dermoscopy for malignancy was high despite the high number of false positive nevi on the 7-point checklist because experts likely gave their dermoscopic diagnoses having clinical images available and with a holistic assessment of dermoscopic images. Sensitivity (95% CIs) for PD of the clinical, dermoscopic, and RCM examination were 100% (80-100%), 85% (62-96%), and 86% (62-96%) and specificity (95% CIs) were 54% (31-75%), 100% (80-100%), and 100% (80-100%), respectively. Clinical examination had 100% sensitivity because all unilateral plaques/patches and erosions were possible PD. Conversely, RCM and dermoscopy had 100% specificity for PD, better than clinical examination. RCM superiority in specificity was predictable because of the ability of this technique to identify Paget cells and spongiosis. Experts diagnosed PD in 86% of cases at RCM, but it should be considered that classic RCM presentation of Paget cells as "round and dark intraepidermal cavities" was found in only half of PD cases (Table II). Although there are no validated dermoscopic criteria for eczema and PD of NAC, it is possible that a more irregular vascular pattern in PD allowed the differential diagnosis with eczema. Interinvestigator agreement in the diagnosis evaluated by Fleiss kappa increased from clinical (poor or moderate) to dermoscopic (moderate) and RCM (excellent) examination. Although our study does not have the ability to draw conclusions about primary melanoma, noninvasive imaging techniques added relevant information and seem to improve the differential diagnosis of PD and eczema.

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Table I. Clinical features of the 131 lesions

	MM	PD	Nevus	Melanosis	SK	Eczema	Miscellaneous*	Total
No. of lesions	3	15	66	7	16	10	14	131
Lesion with histologic examination	3	15	21	2	3	8	13	65
Sex, n (%)								
Male	0	1 (7)	7 (11)	0	5 (31)	2 (20)	0	15 (11)
Female	3 (100)	14 (93)	59 (89)	7 (100)	11 (69)	8 (80)	14 (100)	116 (89)
Patient age, y (SD) [†]								
Mean age, y (SD)	70 (6)	64 (14)	33 (13)	34 (14)	54 (15)	47 (26)	57 (21)	43 (20)
Age range, y	65-77	39-91	8-71	18-54	30-81	16-73	24-91	8-91
Anatomic site, n (%)								
Nipple	0	8 (54)	17 (26)	5 (72)	4 (25)	7 (70)	9 (64)	50 (38)
Areola	3 (100)	2 (13)	44 (67)	1 (14)	12 (75)	3 (30)	2 (14)	67 (51)
Both areola and nipple	0	5 (33)	5 (7)	1 (14)	0	0	3 (22)	14 (11)
Shape, n (%)								
Macule/patch	1 (33)	3 (20)	55 (83)	6 (86)	4 (25)	1 (10)	6 (43)	76 (58)
Papule/nodule/plaque	2 (67)	12 (80)	11 (17)	1 (14)	12 (75)	9 (90)	8 (57)	55 (42)
Presence of pigmentation, n (%)								
Yes	3 (100)	4 (27)	66 (100)	7 (100)	16 (100)	0	5 (36)	101 (77)
No	0	11 (73)	0	0	0	10 (100)	9 (64)	30 (23)
Lesion size, mm (SD)								
Maximum diameter	6 (2)	21 (17)	7 (4)	4 (3)	6 (3)	24 (35)	8 (6)	9 (12)
Size range	5-9	2-50	1-20	1-8	3-10	3-100	2-20	1-100
Time to diagnosis, y (SD)								
Mean time	0.2 (0.2)	1.1 (0.9)	10.6 (12)	2.4 (1.8)	3.4 (3.4)	0.5 (0.5)	0.9 (0.3)	7.4 (10.4)
Dermoscopy	3	13	66	7	15	7	14	125
RCM	2	11	37	6	11	9	9	85
Dermoscopy and RCM	2	9	37	6	10	6	9	79

MM, Melanoma; PD, Paget disease; RCM, reflectance confocal microscopy; SD, standard deviation; SK, seborrheic keratosis.

*One adenoma, 1 angioma, 1 pigmented Bowen disease, 2 erosive adenomatosis of the nipple, 1 epidermal cyst, 2 melanoacanthomas, 1 hematoma, 1 mycosis fungoides, 1 bullous pemphigoid, 1 case of skin xerosis, 1 case of Fordyce granules with histologic examination, and 1 radiodermatitis.

[†]Patients with malignant tumors were older than patients with benign lesions (a mean of 64 years [SD 12.9 years] and range of 39-91 years for malignant tumors and a mean of 38.6 years [SD 17.8 years] and range of 8-91 years for benign lesions; *t* test, *P* < .0001).

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Table II. Dermoscopic and reflectance confocal microscopy features

	Primary MM	MM metastasis	Nevus	Melanosis	SK	Other pigmented lesions	PD	Eczema
No. of lesions with dermoscopic images available	1	2	66	7	15	3	13	7
Dermoscopic criteria of the 7-point checklist, n (%)								
Atypical pigment network (2 pts)	1 (100)	0	17 (25.8)	1 (14.3)	0	1 (33)	0	0
Blue-white veil (2 pts)	1 (100)	1 (50)	18 (27.3)	0	2 (13.3)	1 (33)	0	0
Atypical vascular pattern (2 pts)	1 (100)	0	4 (6.1)	0	1 (6.7)	1 (33)	3 (23.1)	0
Irregular streaks (1 pt)	0	0	4 (6.1)	0	0	1 (33)	0	0
Regression structures (1 pt)	1 (33)	0	9 (13.6)	1 (14.3)	0	1 (33)	6 (46.15)	0
Blotches irregularly distributed (1 pt)	0	0	5 (7.6)	0	0	0	1 (7.7)	0
Irregular dots/globules (1 pt)	0	0	7 (10.6)	0	1 (6.7)	1 (33)	0	0
Lesions with total score ≥ 3	1 (100)	0	16 (24.2)	1 (14.3)	1 (6.7)	1 (33)	2 (15.4)	0
Other dermoscopic criteria, n (%)								
Gray-blue pigmentation	0	1 (50)	17 (25.8)	0	1 (6.7)	1 (33)	1 (7.7)	0
Milia-like cysts	0	0	4 (6.1)	0	2 (13.3)	0	0	0
Comedo-like openings	0	0	1 (1.5)	0	5 (33.3)	0	0	0
Dotted vessels	0	0	0	0	1 (6.7)	0	2 (15.38)	2 (28.57)
Linear vessels	0	1 (50)	0	0	0	0	5 (38.46)	2 (28.57)
Milky-red areas	0	0	0	0	0	0	6 (46.15)	0
No. of lesions with RCM images available	1	1	37	6	11	2	11	9
RCM criteria of the Pellacani et al score, n (%)								
Atypical cells at the DEJ (2 pts)	1 (100)	0	5 (13.5)	0	1 (9)	0	0	0
Nonedged papillae (2 pts)	1 (100)	0	3 (8.1)	0	0	0	1 (9)	0
Roundish pagetoid cells (1 pt)	1 (100)	0	1 (2.7)	0	0	1 (50)	1 (9)	0
Widespread dendritic pagetoid cells (1 pt)	0	0	10 (27)	0	0	0	1 (9)	0
Cerebriform nests (1 pt)	0	0	0	0	0	0	0	0
Nucleated cells within upper dermis (1 pt)	0	1 (100)	0	0	0	0	0	0
Lesions with total score ≥ 3	1 (100)	0	5 (13.5)	0	0	0	0	0
Other RCM criteria, n (%)								
Dark Paget cells	0	0	0	0	0	0	5 (45.5)	0
Spongiosis	0	0	0	0	1 (9)	0	1 (9.1)	6 (66.7)

DEJ, Dermoepidermal junction; MM, Melanoma; PD, Paget disease; pt, point; RCM, reflectance confocal microscopy; SD, standard deviation; SK, seborrheic keratosis.

Dermoscopy was performed at $\times 20$ magnification and RCM images were acquired with VivaScope 3000 (51 cases) or 1500 probe (34 cases) (Caliber Imaging and Diagnostics, Rochester, NY). Only images considered relevant for the diagnosis by an RCM expert were captured by RCM. Images of different depths (epidermis, DEJ, and dermis) were always present.

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A review of smartphone applications for promoting sun protection practices



To the Editor: Primary prevention of skin cancer is best achieved by protecting the skin from exposure to ultraviolet (UV) radiation; exposure to UV radiation increases the risk for both melanoma and nonmelanoma skin cancers.¹ The US Preventive Task Force recommends that children and adults be counseled on using sun protection practices to minimize UV exposure and suggests that mobile smartphone applications might be useful to facilitate these behaviors.² The effectiveness of smartphone applications to promote a variety of health behaviors targeting exercise performance, weight loss, diet, smoking cessation, alcohol consumption, and sun protection has been examined in the published literature.³ Skin cancer prevention is particularly amenable to intervention from smartphone applications by helping individuals monitor UV exposure and provide tailored recommendations and reminders for protecting their skin. Dozens of applications of varying quality are currently available, making it difficult for interested users to find applications with useful, intuitive, and effective features.

The purpose of this study was to provide a comprehensive list of currently available sun protection smartphone applications and their features. In August 2018, we searched the Apple (Cupertino, CA) and Android (Google, Menlo Park, CA) App stores for applications that promote sun protection practices. Search terms included “skin

cancer,” “sun,” “UV protection,” and “melanoma.” Results were screened according to predefined inclusion and exclusion criteria. Smartphone apps were included if they provided specific, personalized advice regarding sun protection using local UV indices and the user's personal skin characteristics. We excluded apps that only provided weather, UV information, or general recommendations and those that were not in English, were country specific, or not for patient use. We also excluded apps that were incompatible with the latest smartphone operating systems and that required purchase of a wearable UV dosimeter. Last, we compared apps on the basis of features that have been shown to improve the effectiveness of apps targeting behavior change, such as having a user-friendly design, providing real-time feedback, and offering tailored advice supplemented by additional information.⁴

Our search revealed 1060 results across both app stores (including duplicates), from which we identified 9 eligible apps (Table 1). Most apps were user friendly, intuitive, and provided personalized sun protection recommendations tailored to user skin type and color. Recommendations included avoiding being outdoors during periods of high UV light, a minimum sunscreen sun protection factor and time until reapplication, and types of physical protection (ie, clothing, hats, and sunglasses). However, we found limited published evidence regarding the effectiveness of these apps for facilitating sun protection behaviors. In fact, only SunZapp developers (Klein Buendel Inc, Golden, CO) provided citations to 3 published studies showing limited improvement in sun protection.⁵ We found most apps included in this review to be easy to use while providing instant feedback and tailored recommendations to users, but only SunSense (Raymio, Copenhagen, Denmark) satisfied all criteria by offering additional information about sun protection. Although we have identified several apps with the potential to promote sun safety, further investigation is required to establish whether their use results in sustained behavior change and reductions in UV exposure. Future research should also consider comparing apps that utilize wearable technology for real-time UV tracking and those that rely on regional UV indices.

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