Dermatology Practical & Conceptual

Indications for and Contraindications to Digital Monitoring of Patients with Melanocytic Lesions

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Addressing melanocytic lesions could be challenging, both in cases of multiple and solitary lesions. For patients with multiple melanocytic nevi, the best approach is periodic total-body photography and digital dermoscopy acquisition with comparisons of the lesions over time. There are some scenarios in which digital monitoring (DM) is indicated even in cases of solitary lesions. Congenital and Spitz nevi are typical examples of solitary lesions that could be monitored thanks to the patient age. Pigmented lesion of the nail unit is another example of a lesion that can be followed up in some cases, as well as the flat pigmented facial macule. Contraindications to monitoring solitary lesions include nodular lesions without clear-cut benign criteria, lesions showing regression patterns, and amelanotic lesions.

This editorial will discuss the following points:

- Indications for monitoring patients with multiple melanocytic nevi
- Indications for monitoring solitary lesions
- Contraindications to monitoring solitary lesions

Indications for Monitoring Patients with Multiple Melanocytic Nevi

The most important indication for DM is the patient with multiple melanocytic nevi. The current approach includes total-body mapping, which consists of photographic documentation of the entire body surface (total-body photography), followed by digital dermoscopy imaging of selected melanocytic lesions. When dealing with a patient with multiple melanocytic lesions, comparison of the sequential images allows us to excise only those showing asymmetrical growth or a significant morphologic change, thus minimizing unnecessary excision of non-changing atypical nevi.

DM is a time-consuming technique primarily accessible in third-level centers; therefore, it is crucial to identify patients who can truly benefit from this approach. Recently, the International Dermoscopy Society (IDS) reached a consensus of experts using the E-Delphy methodology [1]. Based on levels of evidence and previous studies, the experts agreed that DM can be indicated for patients with more than

60 melanocytic nevi in the absence of other melanoma risk factors. In the presence of specific risk factors such as personal history of melanoma, immunodepression, presence of red hair and/or a MC1R mutation, DM can be indicated also for patients with 40 melanocytic nevi or more. Regarding genetic predisposition, DM is strongly indicated in patients with a *CDKN2A* mutation, independent of the number of nevi, as their relative risk of developing a melanoma is considerably high. The latter risk is based on the ratio between the lifetime risk of melanoma in patients with the mutation and the lifetime risk of melanoma in the general population.

In the management of patients who are candidates for DM, the combination of sequential imaging with the comparative approach is considered the gold standard [2]. Comparative approach consists of clinical and dermoscopic examination of all the melanocytic lesions of a given patient in order to find the signature nevus pattern. It is based on the concept that most nevi of an individual share similar clinical and dermoscopic morphologies [2]. Then, sequential DM is combined with the comparative approach, which increases diagnostic sensitivity for early melanoma. In a case-control study [3], on a total of 206 melanomas, almost 60% had been diagnosed only because of the side-by-side image comparison, since none of them developed melanoma-specific criteria after a mean follow up of 15 months (Figure 1).

Indications for Monitoring Solitary Lesions

There are some scenarios in which DM is indicated even in cases of solitary lesions. Given the very low risk of melanoma in childhood, congenital and Spitz nevi are typical examples of solitary lesions that could be monitored due to a patient age. Pigmented lesions of the nail unit are examples of solitary lesions that can be followed up in some cases, as well as flat pigmented facial macules.

Congenital Melanocytic Nevi

Congenital melanocytic nevi (CMN) are benign proliferations usually present at birth or within the first years of life. As size is considered the main criterion to categorize CMN and to predict the clinical outcome, they are classified as small (<1.5 cm), medium (1.5–19.9 cm), and large/giant (>20 cm). The general rule predicts that the larger the diameter, the higher the risk of melanoma development in CMN [4].

However, since giant CMN are very rare, the probability of finding a CMN-associated melanoma is very low. In contrast, due to their higher prevalence, finding a melanoma associated with a small CMN in a real clinical setting is more probable [4]. Medium-size CMN carry a risk for melanoma development of about 0.5%. Their prevalence is much lower than small CMN, although higher than large CMN. In our estimation, medium-size CMN might be managed conservatively or excised. Referring children to surgery could raise practical problems considering the risks related to general anesthesia and the surgical procedure. Therefore, in this category of patients, observation with clinical and dermoscopic follow-up may be considered the best approach (Figure 2).

Spitz Nevi

Spitz nevi (SN) are melanocytic proliferations typically found in children and characterized by morphologic similarity to

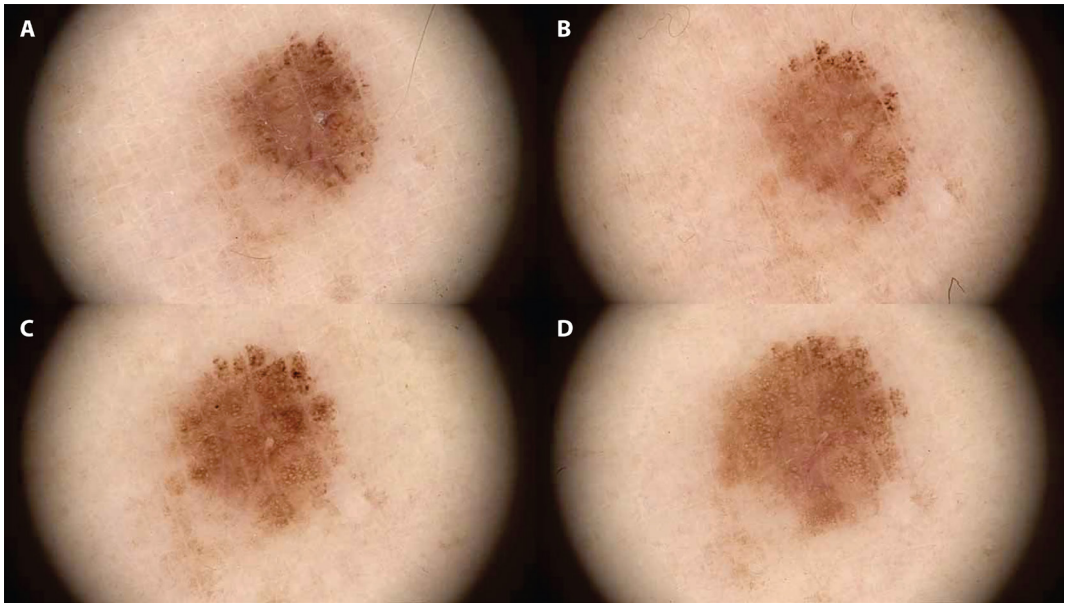

Figure 1. (A-D) Follow-up of a melanocytic lesion from June 2020 (A) to December 2021 (D) (every 6 months). In situ melanoma without clear-cut malignant criteria but excised because of the change over time.

Figure 2. Congenital nevus in a young adult. Follow-up is allowed because of the risk of a scar on the face.

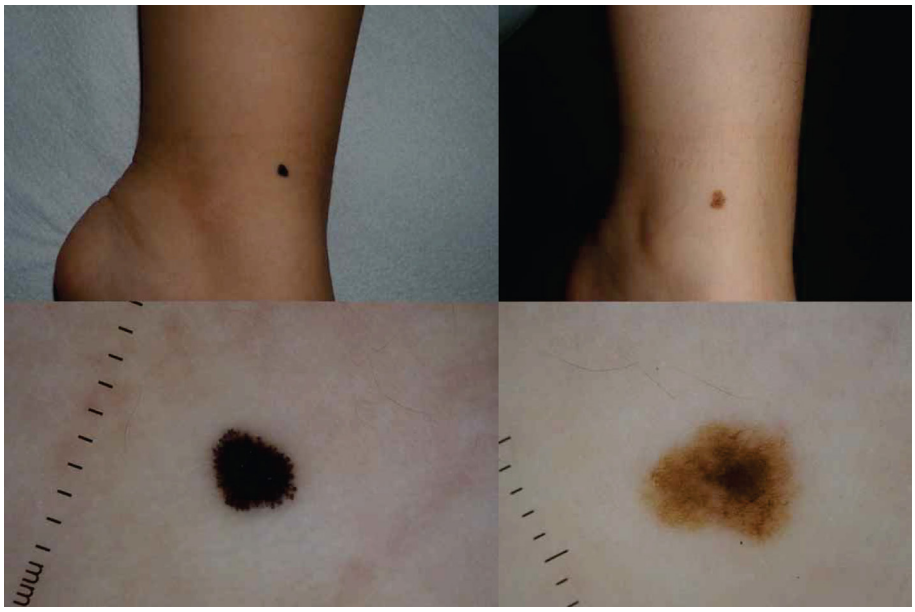

Figure 3. Spitz nevus in a 3-year-old girl pictured at baseline and after 4 years of follow-up: the classic starburst pattern became a reticular one with central hyperpigmentation.

melanoma. From the time of Sophie Spitz [5], the biologic behavior of these lesions has been extensively questioned. The IDS proposed a management workup based on clinical and dermoscopic characteristics of the lesions that allows the clinician to establish the correct management [6]. According to these guidelines, asymmetric lesions with spitzoid features (both flat/raised and nodular) should be excised to rule out melanoma [6]. Even symmetric, spitzoid nodules should be excised or closely monitored, irrespective of age, to rule out atypical Spitz tumors. In contrast, symmetric, flat lesions showing a starburst pattern below the age of 12 years may be monitored over time. Starburst pattern consists of a central area of homogeneous black-blue pigmentation and symmetrically distributed peripheral streaks or pseudopods. Lesions showing starburst pattern are expected to grow, reach stabilization and then involute (Figure 3). During their evolution, these nevi gradually acquire a blue-black homogeneous aspect with disappearance of the peripheral projections. After years, the dark pigmented area will be gradually restricted to the center of the lesion, while the peripheral part of the nevus may exhibit remnants of a delicate brown network resembling the recently described stardust pattern [7].

In conclusion, both congenital nevi and Spitz nevi with typical flat symmetrical findings could be monitored in childhood, with a very low risk of missing a melanoma.

Longitudinal Melanonychia

Longitudinal melanonychia (LoM) is a longitudinal pigmentation of the nail unit derived from the activation of melanocytes or their proliferation in the nail matrix. In the first case, the color is grayish, and etiologies include

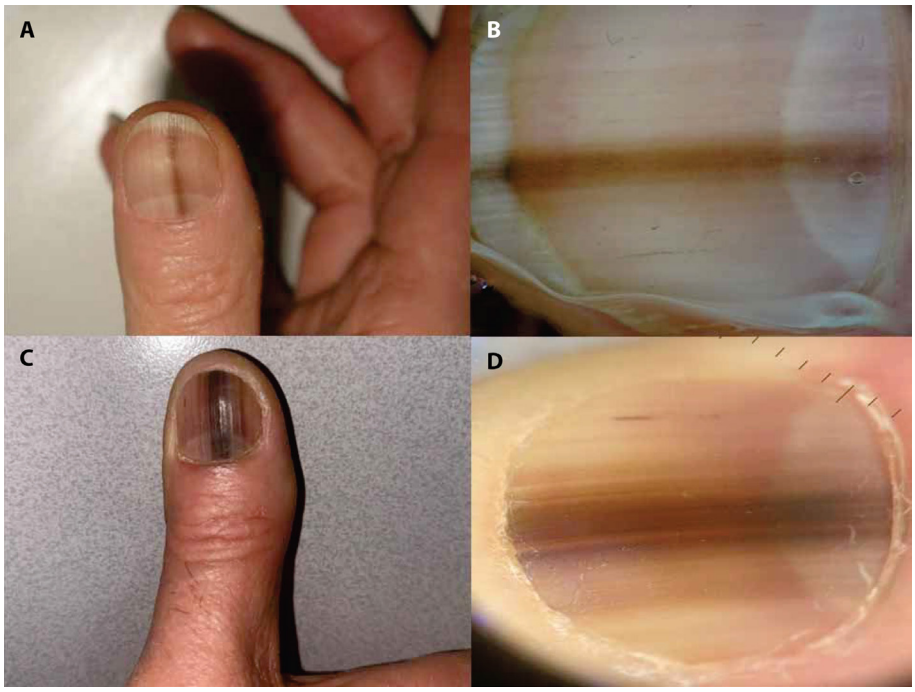

Figure 4. A 47-year-old woman with a nail pigmented band. The patient was not compliant with follow- up and showed up 4 years later (C,D), when the lesion was excised and diagnosed as melanoma in situ.

ethnic pigmentation, trauma, onychotillomania, medication, and genetic syndromes, such as Peutz-Jeghers and Lauzier-Hunziker [8]. When secondary to melanocytic proliferation, the color of LoM is brownish black and the differential diagnosis includes nevus and melanoma.

To distinguish a potentially malignant lesion from a benign one, the adapted ABCDE rule was proposed [9]. Melanoma could be suspected in the fifth to seventh decades of life: A stands for age, and is more likely in African Americans, Asians, and native Americans in whom subungual melanoma accounts for up to one-third of all melanoma cases. B (standing for band) refers to a brown to black band with width of 3 mm or more and variegated borders. C stands for change in the nail band, and D for the digit most commonly involved, namely, the first digit. Finally, E stands for extension of the pigment onto the proximal and/or lateral nailfold (Hutchinson sign).

When dealing with a case of longitudinal melanonychia without alarming criteria, a follow- up could be considered (Figure 4). Nail surgery is a difficult, painful, and potentially scarring procedure. Therefore, monitoring a small pigmented nail band could help in avoiding unnecessary biopsy of stable bands, even though it is possible to improve early diagnosis of melanoma by excising changing and growing pigmented nail bands [10].

There is still no consensus about the follow-up of melanonychia, which requires periodic clinical and dermoscopic photographic documentations. The proposed schedule consists of clinical and dermoscopic examination every 6 months in cases of a regular band, and a 3-month follow-up in cases of irregular pigmentation without other signs of malignancy [11].

Flat Pigmented Facial Lesions

The face represents a challenging area for the differential diagnosis of flat pigmented lesions, as lentigo maligna (LM) shares similar epidemiological, pathogenetic and morphologic characteristics with pigmented actinic keratosis and solar lentigo/flat seborrheic keratosis [12]. LM appears as a solitary macule with asymmetric pigmented follicular openings. The prevalent color is gray, which may be arranged in an annular-granular pattern, rhomboidal structures, and up to obliterated hair follicles [12]. However, it has been demonstrated that these criteria are neither specific nor sensitive [13,14]. To address this diagnostic problem, a new method called "the inverse approach" was introduced [14]. It is based on the absence of non-melanoma prevalent patterns like scales, white and wide follicular openings, erythema, reticular or parallel brown lines, sharply demarcated border and milia-like cysts/comedo-like openings. The absence of a prevalent benign dermoscopic criterion is sufficient to consider the diagnosis of LM. However, LM is a very slow-growing melanoma in situ, thus, in lesions lacking predominant non-melanoma criteria, a follow-up might be considered as a reasonable approach. There is also another reason why follow-up might be indicated in these cases, namely, a very early LM might be a challenge for the pathologist to

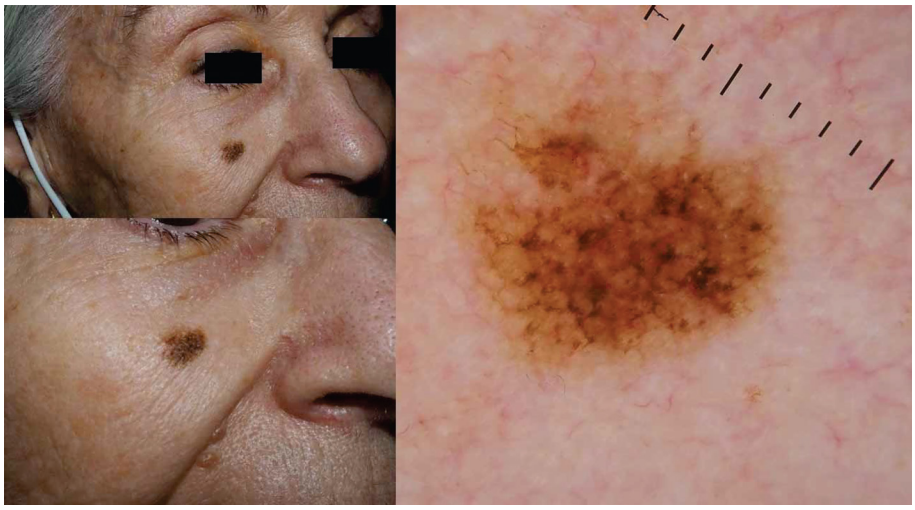

Figure 5. Pigmented macule on the right cheek. Dermoscopy does not show clear-cut benign criteria. Histology posed for in situ melanoma (lentigo maligna).

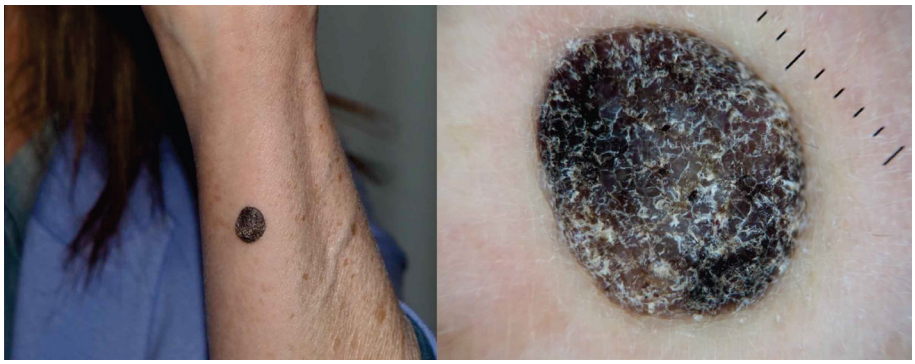

Figure 6. An invasive melanoma (pT1b – AJCC 8 ed.) on the left arm, mimicking seborrheic keratosis.

diagnose. In early LM melanoma-specific histopathologic criteria might be very subtle thus prompting the pathologist to use diagnostic categories such as "atypical junctional melanocytic proliferation" and "junctional nevus" [15-16]. Therefore, careful DM might be useful in acquiring dynamic information of the lesion, without a negative impact on prognosis due to the slow-growing nature of LM (Figure 5) [17].

Contraindications to Monitoring Solitary Lesions

Contraindications to monitoring solitary lesions include nodular lesions without clear-cut benign criteria, lesions showing regression patterns, and amelanotic lesions.

Nodular Lesions Without Clear Cut Benign Criteria

Nodular lesions pose diagnostic problems because nodular melanoma (NM) may simulate different melanocytic and nonmelanocytic tumors such as basal cell carcinoma, squamous cell carcinoma, seborrheic keratosis, dermal nevus, dermatofibromas and vascular lesions, to name but a few (Figure 6) [18].

Several studies have explored the dermoscopic characteristics of pigmented and non-pigmented NM. In the study of Sgouros et al, on a total of 254 lesions, irregular blue structureless areas, dotted vessels, and serpentine vessels were predictors of NM compared to non-melanoma nodular lesions [19]. In another study, the most important features of pigmented NM vs nodular pigmented non-melanomas included peripheral and/or irregular black dots/globules, multiple brown dots, blue-white veil, homogeneous blue pigmentation, 5 to 6 colors, and black color [20].

NM comprises 12%-30% of all melanomas, but it accounts for at least 50% of all melanomas thicker than 2 mm, thus being associated with a poor prognosis in a significant number of cases [19]. Hence, any nodular lesion that cannot be confidently diagnosed as benign should be promptly excised and follow-up should be strongly discouraged.

Lesions Showing Regression Patterns

Regression is a controversial and confounding phenomenon seen in dermoscopy as white scar-like areas or gray structures arranged as peppering or granularity [21]. The histologic correspondence of these blue-white structures (BWS) includes fibrosis and melanophages. Regression is present both in benign and in malignant lesions. Zalaudek et al proposed a flow chart to manage melanocytic lesions exhibiting dermoscopic features of regression [22]. This simple method takes into consideration the extension and location of BWS. They suggest that the presence of irregularly distributed BWS covering more than 50% of the lesion surface favors the diagnosis of melanoma. In contrast, nevi tend to reveal only blue areas in a central location involving less than 50% of the lesion surface. However, as regression is a confounding phenomenon, it is mandatory to avoid follow-up of a solitary lesion exhibiting these patterns (Figure 7).

Amelanotic Lesions

Amelanotic melanoma (AM) accounts for 2%–8% of all melanomas and represents an important diagnostic pitfall for clinicians. It could mimic other melanocytic and non-melanocytic lesions such as basal cell carcinoma, dermal nevus, and pyogenic granuloma, as well as inflammatory conditions as psoriasis or dermatitis.

Regarding dermoscopy for melanomas lacking pigment, it is crucial to analyze the vascular pattern. The most common vascular structures in AM include dotted vessels, serpentine (linear irregular) vessels, or a combination of them (polymorphous vessels). Sometimes peripheral light brown structureless areas are visible, which are more frequently seen in AM as compared to benign melanocytic lesions (Figure 8). As a general rule, AM should be considered in the differential diagnosis when isolated and persistent erythematous lesions are found, even if the lesion does not manifest any of the melanoma ABCD clinical criteria [23].

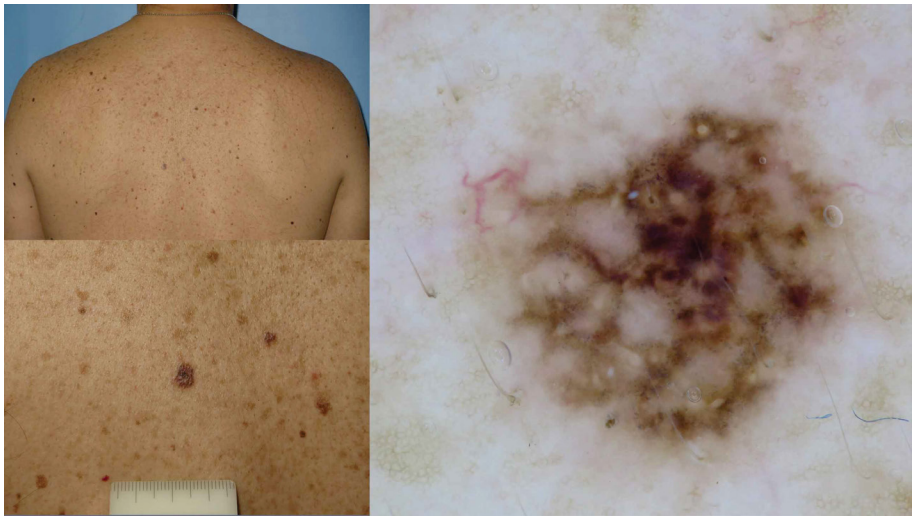

Figure 7. In situ melanoma on the back of a middle-aged man. On dermoscopy, gray granularity and scar-like depigmentation.

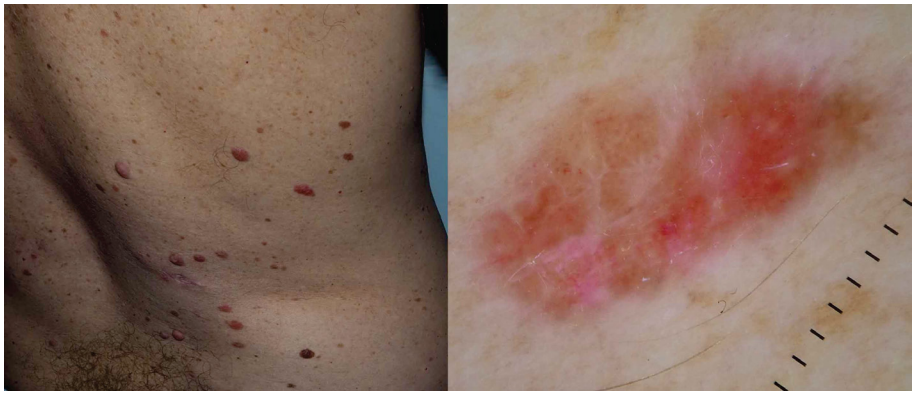

Figure 8. An amelanotic melanoma (pT1b – AJCC 8 ed.) on the back, with polymorphous vessels and light brown structureless areas.

Conclusions

Indications for and contraindications to monitoring melanocytic lesions depend on a number of different factors related to the given patient (age, total nevus count) and the given lesion (morphology, location), and the diagnosis is based on the combination of all these factors that are correlated with a complete clinical and dermoscopic examination.

References

1. Russo T, Piccolo V, Moscarella E, et al. Indications for Digital Monitoring of Patients With Multiple Nevi: Recommendations from the International Dermoscopy Society. *Dermatol Pract Concept.* 2022;12(4):e2022182. DOI: 10.5826/dpc.1204a182. PMID: 36534527. PMCID: PMC9681223.
2. Moscarella E, Tion I, Zalaudek I, et al. Both short-term and long-term dermoscopy monitoring is useful in detecting melanoma in patients with multiple atypical nevi. *J Eur Acad Dermatol Venereol.* 2017;31(2):247-251. DOI: 10.1111/jdv.13840. PMID: 27422807.
3. Babino G, Lallas A, Agozzino M, et al. Melanoma diagnosed on digital dermoscopy monitoring: A side-by-side image comparison is needed to improve early detection. J Am Acad Dermatol. 2021 Sep;85(3):619-625. doi: 10.1016/j.jaad.2020.07.013. Epub 2020 Jul 8. PMID: 32652193.
4. Caccavale S, Calabrese G, Mattiello E. et al. Cutaneous Melanoma Arising in Congenital Melanocytic Nevus: A Retrospective Observational Study. Dermatology. 2021;237(3):473-478. doi: 10.1159/000510221. Epub 2020 Oct 14. PMID: 33053549.
5. SPITZ S. Melanomas of childhood. Am J Pathol. 1948 May; 24(3):591-609. PMID: 18859360; PMCID: PMC1942798.
6. Lallas A, Apalla Z, Ioannides D, et al. Update on dermoscopy of Spitz/Reed naevi and management guidelines by the International Dermoscopy Society. Br J Dermatol. 2017 Sep;177(3):645-655. doi: 10.1111/bjd.15339. Epub 2017 Jul 19. PMID: 28118479.
7. Brunetti B, Briatico G, Scharf C, et al. Stardust Pattern as Evolution of Pigmented Spitz Nevi During Childhood. Dermatol Pract Concept. 2023 Jan 1;13(1):e2023041. doi: 10.5826/dpc.1301a41. PMID: 36892359; PMCID: PMC9946083.
8. Singal A, Bisherwal K. Melanonychia: Etiology, Diagnosis, and Treatment. Indian Dermatol Online J. 2020 Jan 13;11(1):1-11. doi: 10.4103/idoj.IDOJ_167_19. PMID: 32055501; PMCID: PMC7001389.
9. Levit EK, Kagen MH, Scher RK et al. The ABC rule for clinical detection of subungual melanoma. J Am Acad Dermatol. 2000 Feb;42(2 Pt 1):269-74. doi: 10.1016/S0190-9622(00)90137-3. PMID: 10642684.
10. Khan K, Mavanur AA. Longitudinal melanonychia. BMJ Case Rep. 2015 Dec 10;2015:bcr2015213459. doi: 10.1136/bcr-2015-213459. PMID: 26655230; PMCID: PMC4680278.
11. Starace M, Alessandrini A, Brandi N, et al. Use of Nail Dermoscopy in the Management of Melanonychia: Review. Dermatol Pract Concept. 2019 Jan 31;9(1):38-43. doi: 10.5826/dpc.0901a10. PMID: 30775147; PMCID: PMC6368078.
12. Lallas A, Argenziano G, Moscarella E, et al. Diagnosis and management of facial pigmented macules. Clin Dermatol. 2014 Jan-Feb; 32(1):94-100. doi: 10.1016/j.clindermatol.2013.05.030. PMID: 24314382.
13. Tschandl P, Rosendahl C, Kittler H. Dermatoscopy of flat pigmented facial lesions. J Eur Acad Dermatol Venereol. 2015 Jan;29(1):120-7. doi: 10.1111/jdv.12483. Epub 2014 Mar 24. PMID: 24661420.
14. Lallas A, Lallas K, Tschandl P, et al. The dermoscopic inverse approach significantly improves the accuracy of human readers for lentigo maligna diagnosis. J Am Acad Dermatol. 2021 Feb;84(2):381-389. doi: 10.1016/j.jaad.2020.06.085. Epub 2020 Jun 24. PMID: 32592885.
15. Moscarella E, Guitera P, Scolyer RA, et al. Junctional Nevus and Early Melanoma on Sun-Damaged Skin of the Head/Neck: a Clinico-Pathologic Challenge. Dermatol Pract Concept. 2023 Apr 1;13(2):e2023122. doi: 10.5826/dpc.1302a122. Epub ahead of print. PMID: 36947065; PMCID: PMC10188153.
16. Zalaudek I, Cota C, Ferrara G, et al. Flat pigmented macules on sun-damaged skin of the head/neck: junctional nevus, atypical lentiginous nevus, or melanoma in situ? Clin Dermatol. 2014 Jan-Feb;32(1):88-93. doi: 10.1016/j.clindermatol.2013.05.029. PMID: 24314381.
17. Collgros H, Rodriguez-Lomba E, Regio Pereira A, et al. Lentiginous melanoma (lentigo maligna and lentigo maligna melanoma) in Australia: clinicopathological characteristics, management and recurrence rates after 10-year follow-up at a tertiary centre. J Eur Acad Dermatol Venereol. 2021 Jun;35(6):1315-1322. doi: 10.1111/jdv.17135. Epub 2021 Mar 3. PMID: 33502077.
18. Longo C, Farnetani F, Ciardo S, et al. Is confocal microscopy a valuable tool in diagnosing nodular lesions? A study of 140 cases. Br J Dermatol. 2013 Jul;169(1):58-67. doi: 10.1111/bjd.12259. PMID: 23374159.
19. Sgouros D, Lallas A, Kittler H, et al. Dermatoscopic features of thin (≤2 mm Breslow thickness) vs. thick (>2 mm Breslow thickness) nodular melanoma and predictors of nodular melanoma versus nodular non-melanoma tumours: a multicentric collaborative study by the International Dermoscopy Society. J Eur Acad Dermatol Venereol. 2020 Nov;34(11):2541-2547. doi: 10.1111/jdv.16815. Epub 2020 Aug 24. PMID: 32654237; PMCID: PMC8422943.
20. Menzies SW, Moloney FJ, Byth K, et al. Dermoscopic evaluation of nodular melanoma. JAMA Dermatol. 2013 Jun; 149(6):699-709. doi: 10.1001/jamadermatol.2013.2466. PMID: 23553375.
21. Moscarella E, Bombonato C, Pampena R, et al. Pigmented skin lesions displaying regression features: Dermoscopy and reflectance confocal microscopy criteria for diagnosis. Exp Dermatol. 2019 Feb;28(2):129-135. doi: 10.1111/exd.13853. Epub 2019 Jan 14. PMID: 30506970.
22. Zalaudek I, Argenziano G, Ferrara G, et al. Clinically equivocal melanocytic skin lesions with features of regression: a dermoscopic-pathological study. Br J Dermatol. 2004 Jan; 150(1):64-71. doi: 10.1111/j.1365-2133.2004.05657.x. PMID: 14746618.
23. Jaimes N, Braun RP, Thomas L, et al. Clinical and dermoscopic characteristics of amelanotic melanomas that are not of the nodular subtype. J Eur Acad Dermatol Venereol. 2012 May;26(5):591-6. doi: 10.1111/j.1468-3083.2011.04122.x. Epub 2011 May 18. PMID: 21585561.