Personalized melanoma grading system: a presentation of a patient with four melanomas detected over two decades with evolving whole-body imaging and artificial intelligence systems

Rhett Drugge[1], Xhuljeta Naqo[1], Sabina Dedej[2], Galyna Girnyk[3], Jona Naqo[1], Frank Drugge[1], Elgida Volpicelli[4]

Affiliations: [1]Melanoscan LLC, Stamford, Connecticut, USA, [2]University of Medicine, Tirana, Albania, [3]Department of Dermatology and Venereology, Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine, [4]Department of Pathology, Stamford Hospital, Stamford, Connecticut, USA

Corresponding Author: Rhett Drugge, Melanoscan LLC, 50 Glenbrook Road, Unit 1C, Stamford, CT 06902, Tel: 203-253-2988, Email: rhett@drdrugge.com

Abstract

Melanoma is a life-threatening tumor that significantly impacts individuals' health and society worldwide. Therefore, its diagnostic tools must be revolutionized, representing the most remarkable human efforts toward successful management. This retrospective study includes the multidimensional analysis of five melanomas in a man in our clinic including whole-body photography, dermatoscopy, artificial intelligence system, genetic test, and the final histopathological conclusion. The correlation between findings in each diagnostic step is discussed. The value of the melanoma grading system will be the application in high-risk lesions to make the right management decision.

Keywords: artificial intelligence, dermatoscopy, grading system, melanoma, Melanoscan®, tracking, photography, whole-body

Introduction

High-risk melanoma screening aims for accurate results while minimizing false positives and negatives. Our goal was to establish an efficient screening pathway that enhances diagnostic precision, reduces time and cost, and minimizes unnecessary biopsies. Although there is no perfect tool for melanoma detection, evolving techniques, as demonstrated in this case, hold the potential to detect future melanomas at the earliest stage as part of a grading system.

Case Synopsis

In this longitudinal study, we employed a phased, multimodal methodology. The patient, assessed as an optimal candidate for digital monitoring based on International Dermatoscopy Society (IDS) recommendations [1], is a 68-year-old man displaying high compliance with annual whole-body photography examinations over two decades. Phase 1 (2002) methods were based on a standardized survey of skin cancer risk assessment. A baseline scan was obtained and exhibited a deeply invasive melanoma without recording dermatoscopy. In phase 2 (2002-2008), the patient received time-lapse (TL) whole body photography (WBP) annually. Six benign pigmented lesion biopsies were obtained in this era. The most productive examinations in Phase 3 (2008-2018) involved TL WBP and TL dermatoscopy. Eleven melanocytic lesions were biopsied, with four melanomas captured in 2013; spots had been present since the initial WBP in 2002. The fifth melanoma, a new in situ lesion, was found in 2014 (**Figures 1-3**). Phase 4 (2019-2021) and Phase 5 (2022-2023) presented additional artificial intelligence (AI) camera arrays and genomic tape stripping, respectively. No new melanomas were

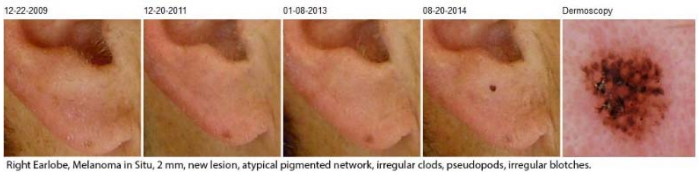

Figure 1. *Right earlobe, new pigmented lesion. Melanoscan images 2009-2014.*

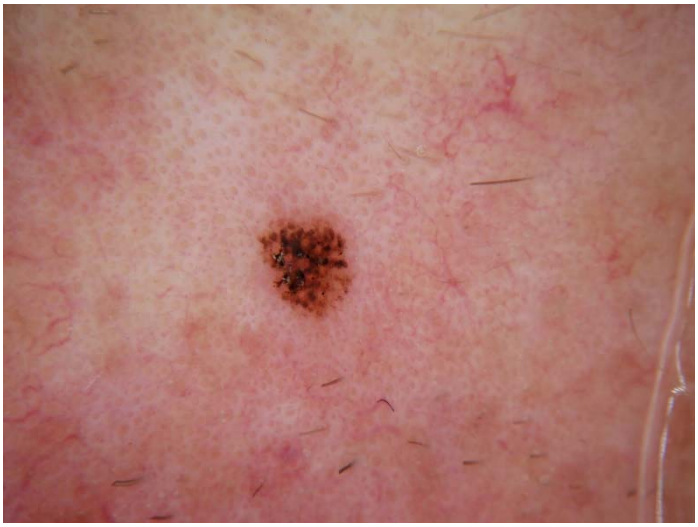

Figure 2. *Dermatoscopy of the melanoma in situ lesion (right earlobe, 2014): 2mm, atypical pigmented network, irregular clods, pseudopods, irregular blotches.*

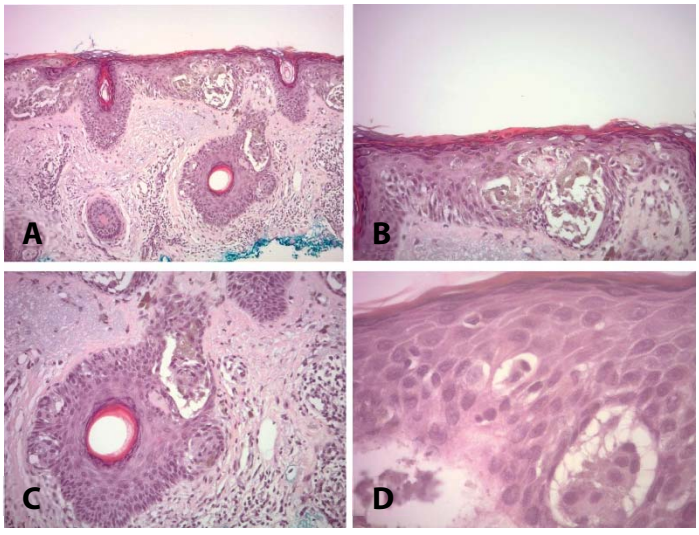

Figure 3. *H&E histopathology.* ***A)*** *Discohesive nests and solitary melanocytes present at all epidermis levels and extend down follicular structures, 100×.* ***B)*** *Discohesive nests that vary in size and shape and solitary epithelioid melanocytes present at all levels of the epidermis, 200×.* ***C)*** *Perifollicular extension, 200×.* ***D)*** *High-power photomicrograph depicting severe cytologic atypia, 630×.*

detected in these periods. Specifically, of six excised lesions, two were Preferentially Expressed Antigen in Melanoma (PRAME) positive lesions, severely dysplastic nevi by pathology, three were PRAME negative and long intergenic non-coding RNA 518 (LINC00518) negative, and one specimen had insufficient quantity to determine.

Case Discussion

Melanoma has the highest mortality rate of all skin cancers, with about 220,000 cases and 37,000 deaths reported annually in the USA and Europe combined [2]. Early recognition of cutaneous melanoma is crucial to avoid human, ethical, and legal consequences.

The field of dermatology has emerged as a forefront domain in integrating and utilizing AI. Convolutional neural networks (CNN) have shown unprecedented accuracy in melanoma recognition [3]. Otherwise, experts can only make correct decisions if they are influenced by a faulty AI [4]. In 2021, we first applied a 7-class CNN for 1,000,212 dermatoscopy images obtained from 2008 as a component of the Melanoscan® system. The dermatoscopy of 251 hotspots identified over two decades in this patient underwent a classifier trained on 10,015 skin lesion images from the public ISIC2018 skin lesion classification dataset, employing both DenseNet and the newer EfficientNet architecture in versions v0 and v0.5, respectively [5,6]. The CNN scores for melanoma are demonstrated in **Table 1**. In this high-risk patient, different AI-pathology correlations (compatible through high scores or incompatible through false high scores) did not introduce superiority compared to the two-step approach (Phase 2). In four melanocytic lesions, we missed AI scores. AI scores were above 0.8 in four melanomas, corresponding to dermatoscopic features. Artificial intelligence demonstrated low scores in three lesions, and in two lesions, AI demonstrated high scores. Similarly, a retrospective study concluded that AI systems could not replace sequential digital dermatoscopy based on sensitivity and specificity evaluation [7].

Ideally, dermatologists aim to use all melanoma screening methods to minimize the number needed to excise lesions (NNEs) and to maximize specificity,

Table 1. *The excised lesions that were suspected of melanoma over two decades.*

Date	Position	Histopathology diagnosis	AI melanoma score /genomic (year)
September 2002	Lower back	Malignant melanoma (3.00 mm)	-
April 2003	Left abdomen	Compound nevus	-
January 2006	Left abdomen	Compound melanocytic nevus, Clark ("dysplastic") type	-
August 2007	Lower back	Compound congenital melanocytic nevus, superficial type.	-
January 2013	Right upper arm	Halo compound lentiginous melanocytic nevus	0.650 (2013)
January 2013	Left mid lateral back	Malignant melanoma in situ - lentigo maligna (arising in conjunction with a small congenital melanocytic nevus)	0.827 (2009), 0.836 (2011), 0.836 (2013)
January 2013	Left popliteal fossa	Malignant melanoma (0.46mm)	0.481 (2009), 0.597 (2011), 0.892 (2013)
February 2013	Right medial leg	Malignant melanoma in situ (lentigo maligna)	0.921 (2013)
August 2014	Right ear lobe	Malignant melanoma in situ	0.923 (2014)
January 2016	Right upper arm	Lentiginous and nested compound melanocytic proliferation with moderate to severe atypia with early regression-like immune response	0.40 (2016)
May 2022	Upper back	Compound melanocytic nevus with moderate to severe atypia	0.84 (2019) LINC00518: negative. PRAME: positive. TERT: negative
May 2022	Right medial thigh	Junctional lentiginous melanocytic nevus with moderate to severe atypia	0.15 (2022)
May 2023	Left helix	Compound melanocytic nevus with moderate atypia	0.079 (2023)
October 2019	Right lower back	Compound melanocytic nevus with moderate atypia arising in a background of pigmented seborrheic keratosis	0.85 (2019)

LINC00518, long intergenic non-coding RNA 518; PRAME, preferentially expressed antigen in melanoma; TERT, telomerase reverse transcriptase.

all while shortening the time of melanoma detection. The number needed to exercise for melanoma diagnosis refers to the number of benign skin lesions that must be removed and evaluated to diagnose one case of melanoma. Various studies have reported multiple NNEs. Kibbie et al. found that the NNEs for melanoma was 6.16 [8]. This is less specific than our result, in which NNEs were 5/14 or 2.8 for melanoma. It is important to note that these numbers may vary depending on the population being screened and other factors. Additionally, the NNE is not a fixed number, and the accuracy of the method used to detect melanoma can be improved over time.

The use of Melanoscan®, a serial, automated, digital whole-body photographic imaging instrument, has shown efficiency in thin melanoma detection [9]. A systematic review concluded that the two-step approach (WBP plus digital monitoring) showed a trend towards a lower Breslow thickness, a higher proportion of in situ melanomas compared to those without WBP, an early detection of melanoma in high-risk populations, and the possibility to integrate AI into 3D WBP systems [10].

State-of-the-art diagnosis of malignant melanocytic lesions relies on histopathologic examination for cases suspicious for melanoma. An innovative non-invasive genomic test that detects genomic

melanoma-associated biomarkers was employed as an additional assay in two lesions before excision in our patient. Only two lesions were PRAME positive but not melanoma histopathologically. Epidermal genetic information retrieval (EGIR) obtains RNA from tape-stripped pigmented lesions discerning melanomas from nevi with 100% sensitivity and 88% specificity [11]. In a recent consensus statement, 86% of respondents were not currently using epidermal tape stripping routinely in their practice, and some panelists believed that clinical use was limited by low specificity. In a hypothetical situation in which epidermal tape stripping had been used to evaluate a suspicious lesion, the panelists agreed that PRAME-positive and LINC-positive (or PRAME-positive only) lesions should be biopsied [12]. The genomic tape stripping can be used to detect melanoma accurately, but further investigations are needed to justify the involvement of this practice in the routine evaluation of melanocytic lesions.

Conclusion

Artificial intelligence classifier scores and genetic test results led to increased biopsies without increased melanoma detections. Melanoma size and thickness decreased over time with increased screening intensity. This may reduce the risk of false negatives and comes at the cost of increased resource utilization. Continued review of the relevance of AI classifier and genomic tape stripping are required. The reality shows that there is no perfect tool for melanoma detection but that today's detection techniques, as applied in this case study, are evolving rapidly and potentially will enable the harvesting of future melanomas at the earliest possible stage as part of the melanoma grading system.

Potential conflicts of interest

The authors declare no conflicts of interest.

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:e2022182. [PMID: 36534527].
2. Cancer Today. Population fact sheets. https://gco.iarc.fr/today/factsheets-populations Accessed on August 9, 2024.
3. Tschandl P. Artificial intelligence for melanoma diagnosis. *Ital J Dermatol Venereol*. 2021;156:289-299. [PMID: 33179882].
4. Tschandl P, Rinner C, Apalla Z, et al. Human-computer collaboration for skin cancer recognition. *Nat Med*. 2020;26:1229-1234. [PMID: 32572267].
5. Jojoa Acosta MF, Caballero Tovar LY, Garcia-Zapirain MB, Percybrooks WS. Melanoma diagnosis using deep learning techniques on dermatoscopic images. *BMC Med Imaging*. 2021;21:6. [PMID: 33407213].
6. Winkler JK, Tschandl P, Toberer F, et al. Monitoring patients at risk for melanoma: May convolutional neural networks replace the strategy of sequential digital dermoscopy? *Eur J Cancer*. 2022;160:180-188. [PMID: 34840028].
7. Kibbie JJ, Zita SM, Dellavalle RP, Dunnick CA, Armstrong CA. The number needed to biopsy for cutaneous melanoma in academic dermatology clinics. *Melanoma Res*. 2024;34:350-354. [PMID: 38934061].
8. Drugge ED, Sarac RM, Elston DM, Drugge RJ. Correlation of total body photography frequency and invasive melanoma depth. *J. Am. Acad. Dermatol*. 2020;82:768-769. [PMID: 31706932].
9. Hornung A, Steeb T, Wessely A, et al. The Value of Total Body Photography for the Early Detection of Melanoma: A Systematic Review. *Int J Environ Res Public Health*. 2021;18:1726. [PMID: 33578996].
10. Wachsman W, Morhenn V, Palmer T, et al. Noninvasive genomic detection of melanoma. *Br J Dermatol*. 2011;164:797-806. [PMID: 21294715].
11. Kashani-Sabet M, Leachman SA, Stein JA, et al. Early Detection and Prognostic Assessment of Cutaneous Melanoma: Consensus on Optimal Practice and the Role of Gene Expression Profile Testing. *JAMA Dermatol*. 2023;159:545-553. [PMID: 36920356].