



Systematic Review Artificial Intelligence Applied to Non-Invasive Imaging Modalities in Identification of Nonmelanoma Skin Cancer: A Systematic Review

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Simple Summary: Artificial intelligence (AI) has shown promise in detecting and diagnosing nonmelanoma skin cancer through image analysis. The incidence of skin cancer continues to rise each year, and it is estimated that one in five Americans will have nonmelanoma skin cancer at some point in their lifetime. Non-invasive diagnostic tools are becoming more widely adopted as the standard of care. When integrated with AI, there is the potential to identify skin cancer earlier and more rapidly compared to traditional methods. This review aims to assess the current status of AI diagnostic algorithms in tandem with noninvasive imaging for the detection of nonmelanoma skin cancer.

Abstract: Background: The objective of this study is to systematically analyze the current state of the literature regarding novel artificial intelligence (AI) machine learning models utilized in noninvasive imaging for the early detection of nonmelanoma skin cancers. Furthermore, we aimed to assess their potential clinical relevance by evaluating the accuracy, sensitivity, and specificity of each algorithm and assessing for the risk of bias. Methods: Two reviewers screened the MEDLINE, Cochrane, PubMed, and Embase databases for peer-reviewed studies that focused on AI-based skin cancer classification involving nonmelanoma skin cancers and were published between 2018 and 2023. The search terms included skin neoplasms, nonmelanoma, basal-cell carcinoma, squamouscell carcinoma, diagnostic techniques and procedures, artificial intelligence, algorithms, computer systems, dermoscopy, reflectance confocal microscopy, and optical coherence tomography. Based on the search results, only studies that directly answered the review objectives were included and the efficacy measures for each were recorded. A QUADAS-2 risk assessment for bias in included studies was then conducted. Results: A total of 44 studies were included in our review; 40 utilizing dermoscopy, 3 using reflectance confocal microscopy (RCM), and 1 for hyperspectral epidermal imaging (HEI). The average accuracy of AI algorithms applied to all imaging modalities combined was 86.80%, with the same average for dermoscopy. Only one of the three studies applying AI to RCM measured accuracy, with a result of 87%. Accuracy was not measured in regard to AI based HEI interpretation. Conclusion: AI algorithms exhibited an overall favorable performance in the diagnosis of nonmelanoma skin cancer via noninvasive imaging techniques. Ultimately, further research is needed to isolate pooled diagnostic accuracy for nonmelanoma skin cancers as many testing datasets also include melanoma and other pigmented lesions.

Keywords: artificial intelligence; dermoscopy; reflectance confocal microscopy; nonmelanoma skin cancer; basal-cell carcinoma; squamous-cell carcinoma; non-invasive imaging; early detection; machine learning



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1. Background

Nonmelanoma skin cancer, primarily basal-cell and squamous-cell carcinoma types, is the most common cutaneous malignancy, accounting for 98% of skin cancers diagnosed [1]. Early detection of skin cancer can reduce morbidity by up to 90% [2]. Traditional skin cancer diagnostic methods can be costly, take time, have potential for resource limitation, and require a well-trained dermatology provider. Non-invasive tools used for diagnosis are increasingly prevalent as a standard of care, particularly for patients with an extensive history of skin cancer. These techniques combined with the application of AI can detect skin cancer early. Thus, AI tools are being increasingly used, including shallow and deep machine learning–based methodologies that are trained to detect and classify skin cancer using computer algorithms and deep neural networks [3]. However, to date, no AI algorithms have been Food and Drug Administration (FDA) cleared (Class II) in the field of dermatology.

As AI becomes increasingly integrated into all computerized functions of medicine and daily activities, it is essential to recognize its potential to assist in computer-directed diagnostics. Utilizing AI, systems can analyze images of skin lesions, pinpointing features indicative of nonmelanoma skin cancer. These systems employ deep learning and convolutional neural networks (CNNs) to train algorithms on extensive datasets of labeled images [4]. An advantage of AI-based nonmelanoma skin cancer imaging lies in its potential for more precise and efficient diagnoses. Dermatology providers can swiftly assess images using AI-based systems, identifying suspicious lesions for further evaluation. Additionally, AI-based nonmelanoma skin cancer imaging holds promise in reducing the necessity for unnecessary, invasive, and costly biopsies. By accurately identifying potentially cancerous lesions, AI-based systems empower dermatologists to target biopsies toward the most concerning areas within a skin lesion.

Numerous studies have proposed innovative designs for skin cancer identification through image analysis [5]. Over time, there has been a growth in computational capabilities through novel and existing approaches, along with expanded datasets for interpretation, leading to robust mathematical models in the current state of AI in the field. Various entities are developing their own AI algorithms for diverse diagnostic modalities and assessing their accuracy [5].

AI is a comprehensive term encompassing computer-aided automated decision-making and is increasingly applied across various aspects of medicine. Machine learning (ML), a subset of AI, involves the use of technologies for data prediction. Subcategories include shallow and deep learning. Both shallow and deep machine learning methods have been trained to identify and classify skin cancer, with algorithms designed to predict malignancies based on patterns found in large datasets of skin lesion images gaining prominence.

This review investigates the utilization of various machine learning mechanisms for non-invasive image analysis. Before delving into our analysis, it is crucial to establish clear definitions for the common terms that will be referenced throughout the discussion.

1.1. Common Machine Learning Methods

As noted above, deep learning is a category of machine learning. This type of algorithm uses machines to interpret and manipulate data from images, speech, or language. Deep learning can be further subcategorized into different types of neural networks. A CNN, or convolutional neural network, is a specialized form of deep neural network (DNN) designed for processing image data. Comprising multiple layers, including convolutional layers, pooling layers, and fully connected layers, CNNs are tailored to efficiently learn features within images [6]. On the other hand, a DNN is a broader category with multiple layers, typically exceeding three, and finds applications in various domains such as image classification, speech recognition, and natural language processing. The key distinction between CNNs and DNNs lies in their approach to processing image data. CNNs are optimized for feature learning in images, employing convolution techniques to extract patterns by sliding a small filter over the image and computing dot products with pixels.

DNNs, in contrast, often use fully connected layers for image processing, linking every neuron in one layer to every neuron in the next, resulting in a larger number of parameters that need optimization during training [6].

Lastly, a deep convolutional neural network (DCNN) is a subtype of CNN with additional layers, enabling it to learn more intricate features and patterns in data. This enhancement contributes to superior performance in tasks like image classification and object detection. The primary difference between CNNs and DCNNs lies in the number of layers, with DCNNs potentially having dozens or even hundreds. While DCNNs offer heightened accuracy, they demand more computational resources and training data, making them more susceptible to overfitting.

1.2. AI Applications in Non-Invasive Imaging Modalities

AI has shown potential in improving the accuracy of nonmelanoma skin cancer diagnosis using dermoscopy and reflectance confocal microscopy (RCM) [3]. Dermoscopy is a non-invasive imaging technique that uses a handheld device to magnify and illuminate skin lesions [1]. AI-based systems can analyze dermoscopy images and identify patterns and features that are indicative of nonmelanoma skin cancer. For example, an AI algorithm can be trained to detect the presence of specific structures, such as white lines, dots, and vascular structures—that are associated with nonmelanoma skin cancer. One advantage of using AI in dermoscopy is the potential for more accurate and efficient diagnoses [5]. Dermoscopy outcomes can be highly user-dependent, leading to variability and poor reproducibility. Applying pattern recognition in deep learning to dermoscopic images can address this concern.

RCM is a non-invasive imaging technique that allows dermatologists to examine skin lesions at a cellular level. It allows in vivo visualization of skin lesions at a nearhistological resolution [5]. It employs a diode laser, and captures horizontal images that are as superficial as the stratum corneum and as deep as the upper dermis. AI-based systems can analyze RCM images to identify patterns and features that are indicative of nonmelanoma skin cancer. For example, an AI algorithm can be trained to detect the presence of abnormal cells, blood vessels, and other features that are characteristic of nonmelanoma skin cancer. On RCM images, numerous studies have applied AI to automatically localize and classify layers of the epidermis [5]. Additional studies have used ML in the detection of the dermal-epidermal junction (DEJ), allowing for immediate visualization of potential malignant features in the DEJ. Applying AI to RCM in skin cancer detection has potential for more reproducible and consistent interpretations of skin architecture. Challenges include diminished image quality due to large RCM files, increased cost and resources, and decreased variability phenotypically. Dermatologists can use AI-based systems to quickly analyze images and identify suspicious lesions that require further evaluation. Additionally, AI-based systems can help reduce inter-observer variability and increase diagnostic accuracy by providing an objective assessment of images.

In this literature review, we sought to collect the latest machine learning algorithms that are being applied to non-invasive diagnostic techniques in nonmelanoma skin cancers. Many algorithms predict the malignancy of pigmented lesions in skin cancer; however, the diagnosis of non-pigmented lesions is generally considered more challenging. To our knowledge, this literature review is the first of its kind to isolate and describe the current state of AI in non-invasive imaging modalities' ability to accurately classify nonmelanoma skin cancers.

2. Materials and Methods

2.1. Search Strategy

Articles published from January 2018–December 2023 were identified from comprehensive searches of MEDLINE, Cochrane, and Embase. Search terms included "skin neoplasms", "diagnostic techniques and procedures", "artificial intelligence", "algorithms", "computer systems", "lesion or growth or cancer or neoplasm or tumor or malignant or metastatic", "carcinoma", "machine or deep learning", "neural network", "diagnosis or detection", "nonmelanoma", "basal-cell carcinoma", "squamous-cell carcinoma", "dermoscopy", "reflectance confocal microscopy", and "optical coherence tomography". Records were screened from MEDLINE, Cochrane, Embase, and Pubmed databases, yielding a total of 967 articles. Prior to initial screening, duplicate articles and articles published prior to 2018 were excluded.

2.2. Study Selection

Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were followed throughout this study. The protocol has not been registered. Search results were evaluated by two independent reviewers, and in the case of a discrepancy in study selection or inclusion criteria, a third reviewer was involved for resolution. Only original, peer-reviewed research manuscripts in the English language were selected for review. We subsequently screened the articles through a review of the title and abstract, with consideration of the research question and appropriate inclusion and exclusion criteria. A total of 317 records were reviewed as full-text articles and considered for inclusion in this review based on our defined inclusion and exclusion criteria. Inclusion criteria included (i) discussion of a novel machine learning algorithm proposal or design, (ii) numerical outcomes reporting the algorithm's accuracy, (iii) an algorithm that completes all steps to diagnosis (not stopping at segmentation, but proceeding to classification), (iv) the study population being human subjects, (v) publication in English, and (vi) the full text being available (Figure 1). Exclusion criteria included articles that (i) failed to address our research question, (ii) utilized invasive techniques for diagnosis, and (iii) screened only based on clinical images (without the use of additional advanced imaging tools).

2.3. Study Analysis

This review systematically evaluated the effectiveness of AI-based methodologies in conjunction with reflectance confocal microscopy, optical coherence tomography, and dermoscopy for detecting nonmelanoma skin cancers. Thus, we elucidated performance metrics including accuracy, sensitivity, specificity, area under the curve (AUC), positive predictive value (PPV), and negative predictive value (NPV). The term "accuracy" refers to the percentage of lesions correctly classified, while "sensitivity" and "specificity" quantify the proportions of true positive and true negative cases, respectively. The AUC comprehensively summarizes the overall performance of the classification model, while the PPV and NPV describe the proportions of lesions accurately reflecting the presence or absence of nonmelanoma skin cancer. By scrutinizing and comparing these performance metrics, we summarized the effectiveness of AI-applied nonmelanoma skin cancer using noninvasive imaging modalities.



Figure 1. PRISMA 2020 flow diagram for new systematic reviews including searches of databases.

3. Results

A total of forty-four articles were selected for review by means of fulfilling our inclusion criteria. Twenty-six of the forty-four articles were published in 2022, five in 2021, and ten in 2020. Prior to 2020, only three articles that were published met our inclusion criteria (Figure 2).



Figure 2. The number of papers per year published included in the literature review.

The majority of the articles described machine learning algorithms used to interpret dermoscopic images (n = 38). Of note, each study utilized variable metrics to quantify the performance of the algorithm. Such metrics included accuracy, precision, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), AUC (area under the curve), and F1 score (Table 1). In each of the reported metrics, a high percentage is correlated with superior algorithm performance.

The most frequently recorded performance metric across studies included in Table 1 was accuracy. Hosny et al.'s convolutional neural network boasted an accuracy of 98.70% [7], which was the highest yielding accuracy of dermoscopy algorithms. Dermoscopy-applied AI detection of NMSC yielded an average accuracy of 86.80% with a standard deviation of 12.05%, a median accuracy of 90.54%, and a minimum accuracy of 37.6%.

Three articles used novel algorithms in association with RCM images, and one used AI applied to hyperspectral epidermal imaging (HEI) (Table 2). Each of the studies applying AI to RCM images reported algorithmic efficacy via different metrics. Wodzinski et al. yielded an accuracy of 87%, Chen et al. reported sensitivity and specificity yielding 100% and 92.4%, respectively, and Campanella et al. recorded an AUC of 86.1% [8–10]. HEI (La Salvia et al.) yielded outcome measures of 87% sensitivity, 88% specificity, and an AUC of 90%, though no reported accuracy [11].

The utilization of diverse image databases for the analysis of AI algorithms showcased additional variability among study designs. Table 3 provides a detailed overview of public dermoscopy image databases that were utilized by studies included in the review.

Lastly, Figure 3 displays the variety of machine learning methods utilized across the studies included in our systematic review. The majority of the studies used CNN as the method for the generation of their machine learning algorithms, with deep learning as the second most common method. DCNNs and DNNs were utilized by a small number of studies, and each of the other papers applied novel, independently generated methods in their algorithms.



Figure 3. Frequency of machine learning techniques used for papers included in our systematic review.

Given the diverse variability of the study design for each included study, a pooled analysis was not able to be calculated. Rather, a QUADAS-2 risk of bias assessment was performed (Table 4). Per QUADAS-2 guidelines, both risk of bias and applicability concerns were evaluated in subcategories including patient selection, index test, reference standard, and flow and timing [12]. None of the studies demonstrated a high risk of bias in any category. However, 11 studies demonstrated high risk of applicability concerns in regard to the index test. No other studies demonstrated high risk of applicability concerns in other categories.

Image Dataset NPV AUC Authors Accuracy Precision Sensitivity Specificity PPV F1 Score Hosny et al. (2020) Internal dataset 98.7% 94.3% 95.1% 94.1% 95.6% 99.39 Xin et al. (2022) [Xin et al. (2022) [HAM1000 Internal dataset 94.1% 94.2% Tang et al. (2022) [14] Skreekala et al. (2022) [15] Seven Point Checklist 74.9% HAM1000 97% Sangers et al. (2022) [16] Samsudin et al. (2022) [17] HAM1000 86.9% 70.4% HAM1000 87.7% ISIC 2019 & 2020 ISIC 2018 ISIC 2019 ISIC 2019 ISIC 2020 S M et al. (2022) [1 Reis et al. (2022) [1 96.8% * 94.6% Reis et al. (2022) [19] Reis et al. (2022) [19] 91.9% 90.5% Razzak et al. (2022) [17] Razzak et al. (2022) [20 Qian et al. (2022) [21] ISIC 2018 HAM1000 98.1% 96.4% 91.6% 73.5%97.1% Popescu et al. (2022) [22] Nguyen et al. (2022) [23] ISIC 2018 HAM1000 86.7% 90% 99% 81% 81% Naeem et al. (2022) [24] Li et al. (2022) [25] 96.9% ISIC 2019 HAM1000 95.8% 96.1% 95 7% Lee et al. (2022) [2 ISIC 2018 84.4% 92.8% 78.5% 91.2% Laverde-Saad et al. (2022) HAM1000 77.1% 80% 86% 86% 80% La Salvia et al. (2022) [28] HAM1000 >80% >80% >80% Hosny et al. (2022) [29] 91.2% 95.3% 94.7% 94.1% 91.4% * Several datasets 91.1% Dascalu et al. (2022) [30] Internal dataset 88% 58.8% Combalia et al. (2019) [31 HAM1000 ISIC 2019 HAM1000 Benyahia et al. (2022) 92.3% Bechelli et al. (2022) 88% Bechelli et al. (2022) HAM1000 72% 95.4% Afza et al. (2022) Ph2 Afza et al. (2022) ISBI2016 91.1% Afza et al. (2022) HAM1000 85.5% Afza et al. (2022) HAM1000 93.4% Afza et al. (2022) ISIC2018 94.4% 70% Winkler et al. (2021) Pacheco et al. (2021) HAM1000 69.2% 70.6% HAM1000 HAM1000 77.1% 85.3% Minagawa et al. (2021) [38] Iqbal et al. (2021) [HAM1000 HAM1000 99.1% Huang et al. (2021) [Zhang et al. (2020) [84.8%DermIS & Dermquest 91% 84% 95% 92% 95% 80% Wang et al. (2020) [42] Qin et al. (2020) [43] Several datasets 100% HAM1000 83.2% 74.3% Maĥbod et al. (2020) [44] Li et al. (2020) [45] ISIC2019 86.2% HAM1000 91% 87% 78%Gessert et al. (2020) [46 Gessert et al. (2020) [47 HAM1000 70% 53% * 97.5% * 94% * Internal dataset Al-masni et al. (2020) [48 Ameri et al. (2020) [49] 89.3% [48]HAM1000 HAM1000 84% 81% Tschandl et al. (2019) [50] Dascalu et al. (2019) [51] Internal dataset HAM1000 80.5% 91.7% 37.6% 41.8% 59.9% 81.4%

Table 1. Summary of included studies utilizing dermoscopy images.

Items with an asterisk (*) represent averaged values. Shaded boxes indicate that a specific measure was not collected in the study.

Table 2. Summary of included studies utilizing imaging modalities other than dermoscopy.

Authors	Imaging Modality	Accuracy	Sensitivity	Specificity	AUC
Wodzinski et al. (2019) [8]	RCM	87%			
Chen et al. (2022) [9]	RCM		100% (when combined with RS)	92.4% (when combined with RS)	
Campanella et al. (2022) [10]	RCM			· · · · · · · · · · · · · · · · · · ·	86.1%
La Ŝalvia et al. (2022) [11]	HEI		87%	88%	90%

Shaded boxes indicate that a specific measure was not collected in the study.

Database	Image Type	Total Images	Description of Dataset
HAM1000	Dermoscopy	10,015	Melanoma (MM)—1113 images Vascular—142 images Benign nevus (MN)—6705 images Dermatofibroma (DF)—115 images Seborrheic keratosis (SK)—1099 Basal-cell carcinoma (BCC)—514 images Actinic keratosis (AK)—327 images
Xin et al. [13] Internal	Dermoscopy	1016	BCC—630 images Squamous-cell carcinoma (SCC)—192 images MM—194 images
SPC	Dermoscopy	>2000	MM, BCC, SK, DF, solar lentigo (SL), vascular, SK Note: Distribution of number of images per lesion type varies in the literature.
ISIC 2016	Dermoscopy	1279	Distribution of number of images per lesion type not readily available
ISIC 2017	Dermoscopy	2000	MM—374 images SK—254 images Other/unknown—1372 images
ISIC 2018	Dermoscopy	10,015	MM—1113 images MN—6705 images BCC—514 images AK—327 images SK—1099 images DF—115 images Vascular—142 images
ISIC 2019	Dermoscopy	25,331	MM—4522 images MN—12,875 images BCC—3323 images AK—867 images DF—239 images SK—2624 images SCC—628 images Vascular—253 images
ISIC 2020	Dermoscopy	33,126	MM—584 images AMN—1 image Café-au-lait macule—1 image SL—44 Lichenoid keratosis—37 images Other/unknown—27124 images
PH2	Dermoscopy	200	Not available

Table 3. Description of databases tested.

Table 4. Summary of QUADAS-2 analysis.

_	Risk of Bias				Applicability Concerns		
Categories	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Low Risk High Risk Unclear/Moderate	27/44 0/44 17/44	31/44 0/44 13/44	42/44 0/44 2/44	44/44 0/44 0/44	20/44 10/44 14/44	37/44 0/44 7/44	$44/44 \\ 0/44 \\ 0/44$

4. Discussion

AI facilitates more accurate triage and diagnosis of skin cancer through digital image analysis, empowering dermatologists [52]. Various techniques, including machine learning, deep learning, and CNNs, are employed in AI-based skin cancer detection. These methods utilize labeled image datasets to train algorithms, enabling them to recognize patterns and features indicative of skin cancer in lesions [2].

AI exhibits significant promise in the detection of skin cancer, yet ongoing efforts to optimize its potential are evident in the trajectory of publication years. The decline in publications in 2021 may be attributed to pandemic-related limitations on resources and the ability to generate novel machine learning algorithms.

Compared to traditional methods, AI-based skin cancer detection offers several advantages. Firstly, AI algorithms swiftly analyze large image datasets, providing dermatologists with more accurate and timely diagnoses. Secondly, these systems reduce the necessity for unnecessary and invasive biopsies, cutting down on costs. Thirdly, AI-based systems can be deployed in remote or underserved areas where access to dermatologists is limited [1].

The reported average diagnostic accuracy of 86.80% when AI is applied to dermoscopic images and a diagnostic accuracy of 87% for RCM-based AI are promising indicators of automated image interpretation potential. However, the wide standard deviation and variability between the minimum accuracy of 37.6% and a maximum of 98.7% in AI applied to dermoscopy underscore the need for further standardization and broader accuracy improvement efforts.

There is a lack of literature on the application of AI to OCT in human lesions. While Ho et al. utilized deep learning for SCC detection in mice, achieving 80% accuracy, there are currently no AI algorithms in the literature for detecting NMSC via OCT in humans [53].

4.1. Limitations

Our QUADAS-2 assessment of bias demonstrates that "patient selection" was unsatisfactory in many of the studies included in this review. This is because the images tested and trained on these AI models frequently utilized public databases of dermoscopy images. Many of these datasets accessible to the public have insufficient sample sizes, thus impacting an AI algorithm's ability to train and reprogram itself [12].

Moreover, imbalanced datasets pose a common challenge for AI models, especially in supervised machine learning where the algorithm is trained on labeled data. Imbalanced datasets arise when there is an unequal distribution of examples among different classes, leading to a skewed representation of certain classes compared to others. For instance, in the context of skin cancer, variations in the incidence of each skin cancer type and a higher percentage of the population with no skin cancer (referred to as "healthy" individuals) contribute to imbalanced datasets. If the training data for the AI model predominantly consists of healthy individuals, it may struggle to accurately predict rarer diseases due to the lack of relevant examples [54].

The primary drawback of imbalanced datasets for AI models is their potential to produce biased and inaccurate results. The model might exhibit a bias toward the majority class, leading to subpar performance on the minority class. In extreme cases, the model might disregard the minority class entirely, resulting in complete misclassification.

In the classification of skin cancer images, this imbalance can be particularly problematic for individuals with darker skin tones, as there is insufficient diversity in skin tone inputs. Existing AI models have mainly been trained on European or East Asian populations, and the limited representation of darker skin tones may compromise overall diagnostic accuracy. This can introduce bias toward Fitzpatrick skin types 4–6, making the model less adept at recognizing or interpreting images of individuals with darker skin tones compared to those with lighter skin tones [55]. Additionally, AI models may rely on color contrast as a pivotal factor in image interpretation, which could lead to misinterpretation due to lower contrast between darker skin tones and other colors compared to lighter skin tones. These limitations carry significant implications for the accuracy and fairness of AI applications across various fields. Therefore, it is essential to ensure that AI models undergo training on diverse datasets and are systematically tested for biases to ensure accurate results and equitable access to emerging health technologies [56].

Furthermore, the efficacy of AI is heavily influenced by image quality, and various factors contribute to variability in this aspect. Differences in image acquisition and quality present a barrier to the implementation of AI in the clinical setting that must be overcome. Achieving consistent, high-quality images necessitates addressing issues such as artifact removal (e.g., hairs, surgical ink markings) and ensuring attention to zoom level, focus, and lighting.

4.2. Future Directions

Future directions may consider automated identification of pigmented lesions, detection of different architectural patterns to distinguish malignant versus benign lesions, categorization of lesions as melanoma versus nonmelanoma skin cancer, and identification of individual skin cells or nuclei using machine learning technologies. It is important to note that the application of AI in dermatology is not a threat to a dermatologist's livelihood—it can be an asset. AI does not devalue the utility of dermatologists, but rather enables a better allocation of their time. Redirecting this finite time can allow for more time spent with patients, increase accessibility to dermatologists, and may increase the accuracy and reproducibility of non-invasive imaging techniques.

5. Conclusions

Overall, AI has the potential to revolutionize the field of skin cancer detection by improving diagnostic accuracy and reproducibility, leading to earlier detection and better outcomes for patients. A high risk of bias and applicability concerns was observed in several of the included studies analyzed via QUADAS-2 assessment. Furthermore, a moderate risk of bias and applicability concerns was observed among many studies. This indicates a need for further standardized evaluation metrics to reduce these biases in studies evaluating diagnostic accuracy. It is also important to note that AI-based skin cancer detection is still in its early stages, and more research is needed to fully evaluate its accuracy and effectiveness, as well as to streamline measures of efficacy. Lastly, AI-based systems should be used as an adjunct stand-alone tool to support dermatologists in their diagnosis rather than as a replacement for human expertise. Ultimately it is the responsibility of the dermatology provider to make an independent decision on how to properly manage their own patients while considering the ancillary information provided by the use of technology such as AI.

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References

- 1. Du-Harpur, X.; Watt, F.M.; Luscombe, N.M.; Lynch, M.D. What is AI? Applications of artificial intelligence to dermatology. *Br. J. Dermatol.* **2020**, *183*, 423–430. [CrossRef]
- Popescu, D.; El-Khatib, M.; El-Khatib, H.; Ichim, L. New Trends in Melanoma Detection Using Neural Networks: A Systematic Review. Sensors 2022, 22, 496. [CrossRef]
- Takiddin, A.; Schneider, J.; Yang, Y.; Abd-Alrazaq, A.; Househ, M. Artificial Intelligence for Skin Cancer Detection: Scoping Re-view. J. Med. Internet Res. 2021, 23, e22934. [CrossRef] [PubMed]
- Das, K.; Cockerell, C.J.; Patil, A.; Pietkiewicz, P.; Giulini, M. Machine Learning and Its Application in Skin Cancer. Int. J. Environ. Res. Public Health 2021, 18, 13409. [CrossRef] [PubMed]
- Patel, R.H.; Foltz, E.A.; Witkowski, A.; Ludzik, J. Analysis of Artificial Intelligence-Based Approaches Applied to Non-Invasive Imaging for Early Detection of Melanoma: A Systematic Review. *Cancers* 2023, 15, 4694. [CrossRef]
- Alzubaidi, L.; Zhang, J.; Humaidi, A.J.; Al-Dujaili, A.; Duan, Y.; Al-Shamma, O.; Santamaría, J.; Fadhel, M.A.; Al-Amidie, M.; Farhan, L. Review of deep learning: Concepts, CNN architectures, challenges, applications, future directions. *J. Big Data* 2021, *8*, 53. [CrossRef] [PubMed]

- Hosny, K.M.; Kassem, M.A.; Fouad, M.M. Classification of Skin Lesions into Seven Classes Using Transfer Learning with AlexNet. J. Digit. Imaging 2020, 33, 1325–1334. [CrossRef] [PubMed]
- Wodzinski, M.; Skalski, A.; Witkowski, A.; Pellacani, G.; Ludzik, J. Convolutional Neural Network Approach to Classify Skin Lesions Using Reflectance Confocal Microscopy. In Proceedings of the 2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Berlin, Germany, 23–27 July 2019; pp. 4754–4757. [CrossRef]
- Chen, M.; Feng, X.; Fox, M.C.; Reichenberg, J.S.; Lopes, F.C.; Sebastian, K.R.; Markey, M.K.; Tunnell, J.W. Deep learning on reflectance confocal microscopy improves Raman spectral diagnosis of basal cell carcinoma. *J. Biomed. Opt.* 2022, 27, 065004. [CrossRef] [PubMed]
- Campanella, G.; Navarrete-Dechent, C.; Liopyris, K.; Monnier, J.; Aleissa, S.; Minhas, B.; Scope, A.; Longo, C.; Guitera, P.; Pellacani, G.; et al. Deep Learning for Basal Cell Carcinoma Detection for Reflectance Confocal Microscopy. *J. Investig. Dermatol.* 2022, 142, 97–103. [CrossRef] [PubMed]
- La Salvia, M.; Torti, E.; Leon, R.; Fabelo, H.; Ortega, S.; Balea-Fernandez, F.; Martinez-Vega, B.; Castaño, I.; Almeida, P.; Carretero, G.; et al. Neural Networks-Based On-Site Dermatologic Diagnosis through Hyperspectral Epi-dermal Images. *Sensors* 2022, 22, 7139. [CrossRef]
- Whiting, P.F.; Rutjes, A.W.; Westwood, M.E.; Mallett, S.; Deeks, J.J.; Reitsma, J.B.; Leeflang, M.M.; Sterne, J.A.; Bossuyt, P.M.; QUADAS-2 Group. QUADAS-2: A revised tool for the quality assessment of diagnostic accuracy studies. *Ann. Intern. Med.* 2011, 155, 529–536. [CrossRef]
- 13. Xin, C.; Liu, Z.; Zhao, K.; Miao, L.; Ma, Y.; Zhu, X.; Zhou, Q.; Wang, S.; Li, L.; Yang, F.; et al. An improved transformer network for skin cancer classification. *Comput. Biol. Med.* 2022, 149, 105939. [CrossRef]
- 14. Tang, P.; Yan, X.; Nan, Y.; Xiang, S.; Krammer, S.; Lasser, T. FusionM4Net: A multi-stage multi-modal learning algorithm for multi-label skin lesion classification. *Med. Image Anal.* **2022**, *76*, 102307. [CrossRef]
- Sreekala, K.; Rajkumar, N.; Sugumar, R.; Sagar, K.V.; Shobarani, R.; Krishnamoorthy, K.P.; Saini, A.K.; Palivela, H.; Yeshitla, A. Skin Diseases Classification Using Hybrid AI Based Localization Approach. *Comput. Intell. Neurosci.* 2022, 2022, 6138490. [CrossRef]
- Sangers, T.; Reeder, S.; van der Vet, S.; Jhingoer, S.; Mooyaart, A.; Siegel, D.M.; Nijsten, T.; Wakkee, M. Validation of a Market-Approved Artificial Intelligence Mobile Health App for Skin Cancer Screening: A Prospective Multicenter Diagnostic Accuracy Study. *Dermatology* 2022, 238, 649–656. [CrossRef]
- 17. Samsudin, S.S.; Arof, H.; Harun, S.W.; Abdul Wahab, A.W.; Idris, M.Y.I. Skin lesion classification using multi-resolution empirical mode decomposition and local binary pattern. *PLoS ONE* **2022**, *17*, e0274896. [CrossRef]
- 18. S M, J.; P, M.; Aravindan, C.; Appavu, R. Classification of skin cancer from dermoscopic images using deep neural network architectures. *Multimed. Tools Appl.* **2023**, *82*, 15763–15778. [CrossRef]
- Reis, H.C.; Turk, V.; Khoshelham, K.; Kaya, S. InSiNet: A deep convolutional approach to skin cancer detection and segmentation. *Med. Biol. Eng. Comput.* 2022, 60, 643–662. [CrossRef] [PubMed]
- Razzak, I.; Naz, S. Unit-Vise: Deep Shallow Unit-Vise Residual Neural Networks with Transition Layer For Expert Level Skin Cancer Classification. *IEEE/ACM Trans. Comput. Biol. Bioinform.* 2022, 19, 1225–1234. [CrossRef] [PubMed]
- 21. Qian, S.; Ren, K.; Zhang, W.; Ning, H. Skin lesion classification using CNNs with grouping of multi-scale attention and class-specific loss weighting. *Comput. Methods Programs Biomed.* **2022**, 226, 107166. [CrossRef] [PubMed]
- 22. Popescu, D.; El-Khatib, M.; Ichim, L. Skin Lesion Classification Using Collective Intelligence of Multiple Neural Networks. *Sensors* 2022, 22, 4399. [CrossRef]
- 23. Nguyen, V.D.; Bui, N.D.; Do, H.K. Skin Lesion Classification on Imbalanced Data Using Deep Learning with Soft Attention. *Sensors* 2022, 22, 7530. [CrossRef]
- 24. Naeem, A.; Anees, T.; Fiza, M.; Naqvi, R.A.; Lee, S.W. SCDNet: A Deep Learning-Based Framework for the Multiclassification of Skin Cancer Using Dermoscopy Images. *Sensors* 2022, 22, 5652. [CrossRef]
- 25. Li, H.; Li, W.; Chang, J.; Zhou, L.; Luo, J.; Guo, Y. Dermoscopy lesion classification based on GANs and a fuzzy rank-based ensemble of CNN models. *Phys. Med. Biol.* 2022, *67*, 185005. [CrossRef]
- 26. Lee, J.R.H.; Pavlova, M.; Famouri, M.; Wong, A. Cancer-Net SCa: Tailored deep neural network designs for detection of skin cancer from dermoscopy images. *BMC Med Imaging* **2022**, *22*, 143. [CrossRef]
- Laverde-Saad, A.; Jfri, A.; Garcia, R.; Salgüero, I.; Martínez, C.; Cembrero, H.; Roustán, G.; Alfageme, F. Discriminative deep learning based benignity/malignancy diagnosis of dermatologic ultrasound skin lesions with pretrained artificial intelligence architecture. *Skin. Res. Technol.* 2022, *28*, 35–39. [CrossRef]
- La Salvia, M.; Torti, E.; Leon, R.; Fabelo, H.; Ortega, S.; Martinez-Vega, B.; Callico, G.M.; Leporati, F. Deep Convolutional Generative Adversarial Networks to Enhance Artificial Intelligence in Healthcare: A Skin Cancer Application. *Sensors* 2022, 22, 6145. [CrossRef] [PubMed]
- 29. Hosny, K.M.; Kassem, M.A. Refined Residual Deep Convolutional Network for Skin Lesion Classification. J. Digit. Imaging 2022, 35, 258–280. [CrossRef] [PubMed]
- Dascalu, A.; Walker, B.N.; Oron, Y.; David, E.O. Non-melanoma skin cancer diagnosis: A comparison between dermoscopic and smartphone images by unified visual and sonification deep learning algorithms. *J. Cancer Res. Clin. Oncol.* 2022, 148, 2497–2505. [CrossRef] [PubMed]

- 31. Combalia, M.; Codella, N.; Rotemberg, V.; Carrera, C.; Dusza, S.; Gutman, D.; Helba, B.; Kittler, H.; Kurtansky, N.R.; Liopyris, K.; et al. Validation of artificial intelligence prediction models for skin cancer diagnosis using dermoscopy images: The 2019 International Skin Imaging Collaboration Grand Challenge. *Lancet Digit. Health* **2022**, *4*, e330–e339. [CrossRef] [PubMed]
- 32. Benyahia, S.; Meftah, B.; Lezoray, O. Multi-features extraction based on deep learning for skin lesion classification. *Tissue Cell* **2022**, 74, 101701. [CrossRef]
- Bechelli, S.; Delhommelle, J. Machine Learning and Deep Learning Algorithms for Skin Cancer Classification from Dermoscopic Images. *Bioengineering* 2022, 9, 97. [CrossRef] [PubMed]
- Afza, F.; Sharif, M.; Mittal, M.; Khan, M.A.; Jude Hemanth, D. A hierarchical three-step superpixels and deep learning framework for skin lesion classification. *Methods* 2022, 202, 88–102. [CrossRef] [PubMed]
- 35. Afza, F.; Sharif, M.; Khan, M.A.; Tariq, U.; Yong, H.S.; Cha, J. Multiclass Skin Lesion Classification Using Hybrid Deep Features Selection and Extreme Learning Machine. *Sensors* **2022**, *22*, 799. [CrossRef] [PubMed]
- 36. Winkler, J.K.; Sies, K.; Fink, C.; Toberer, F.; Enk, A.; Abassi, M.S.; Fuchs, T.; Blum, A.; Stolz, W.; Coras-Stepanek, B.; et al. Collective human intelligence outperforms artificial intelligence in a skin lesion classification task. *J. Dtsch. Dermatol. Ges.* **2021**, *19*, 1178–1184. [CrossRef] [PubMed]
- Pacheco, A.G.C.; Krohling, R.A. An Attention-Based Mechanism to Combine Images and Metadata in Deep Learning Models Applied to Skin Cancer Classification. *IEEE J. Biomed. Health Inf.* 2021, 25, 3554–3563. [CrossRef]
- Minagawa, A.; Koga, H.; Sano, T.; Matsunaga, K.; Teshima, Y.; Hamada, A.; Houjou, Y.; Okuyama, R. Dermoscopic diagnostic performance of Japanese dermatologists for skin tumors differs by patient origin: A deep learning convolutional neural network closes the gap. J. Dermatol. 2021, 48, 232–236. [CrossRef] [PubMed]
- Iqbal, I.; Younus, M.; Walayat, K.; Kakar, M.U.; Ma, J. Automated multi-class classification of skin lesions through deep convolutional neural network with dermoscopic images. *Comput. Med. Imaging Graph.* 2021, 88, 101843. [CrossRef] [PubMed]
- Huang, K.; Jiang, Z.; Li, Y.; Wu, Z.; Wu, X.; Zhu, W.; Chen, M.; Zhang, Y.; Zuo, K.; Li, Y.; et al. The Classification of Six Common Skin Diseases Based on Xiangya-Derm: Development of a Chinese Database for Artificial Intelligence. *J. Med. Internet Res.* 2021, 23, e26025. [CrossRef]
- 41. Zhang, L.; Gao, H.J.; Zhang, J.; Badami, B. Optimization of the Convolutional Neural Networks for Automatic Detection of Skin Cancer. *Open Med.* 2020, 15, 27–37. [CrossRef]
- Wang, S.Q.; Zhang, X.Y.; Liu, J.; Tao, C.; Zhu, C.Y.; Shu, C.; Xu, T.; Jin, H.Z. Deep learning-based, computer-aided classifier developed with dermoscopic images shows comparable performance to 164 dermatologists in cutaneous disease diagnosis in the Chinese population. *Chin. Med. J.* 2020, 133, 2027–2036. [CrossRef]
- 43. Qin, Z.; Liu, Z.; Zhu, P.; Xue, Y. A GAN-based image synthesis method for skin lesion classification. *Comput. Methods Programs Biomed.* **2020**, 195, 105568. [CrossRef]
- 44. Mahbod, A.; Schaefer, G.; Wang, C.; Dorffner, G.; Ecker, R.; Ellinger, I. Transfer learning using a multi-scale and multi-network ensemble for skin lesion classification. *Comput. Methods Programs Biomed.* **2020**, *193*, 105475. [CrossRef]
- Li, C.X.; Fei, W.M.; Shen, C.B.; Wang, Z.Y.; Jing, Y.; Meng, R.S.; Cui, Y. Diagnostic capacity of skin tumor artificial intelligenceassisted decision-making software in real-world clinical settings. *Chin. Med. J.* 2020, 133, 2020–2026. [CrossRef]
- Gessert, N.; Sentker, T.; Madesta, F.; Schmitz, R.; Kniep, H.; Baltruschat, I.; Werner, R.; Schlaefer, A. Skin Lesion Classification Using CNNs with Patch-Based Attention and Diagno-sis-Guided Loss Weighting. *IEEE Trans. Biomed. Eng.* 2020, 67, 495–503. [CrossRef] [PubMed]
- 47. Gessert, N.; Nielsen, M.; Shaikh, M.; Werner, R.; Schlaefer, A. Skin lesion classification using ensembles of multi-resolution EfficientNets with meta data. *MethodsX* **2020**, *7*, 100864. [CrossRef] [PubMed]
- Al-Masni, M.A.; Kim, D.H.; Kim, T.S. Multiple skin lesions diagnostics via integrated deep convolutional networks for segmentation and classification. *Comput. Methods Programs Biomed.* 2020, 190, 105351. [CrossRef] [PubMed]
- 49. Ameri, A. Deep Learning Approach to Skin Cancer Detection in Dermoscopy Images. J. Biomed. Phys. Eng. 2020, 10, 801–806. [CrossRef] [PubMed]
- Tschandl, P.; Rosendahl, C.; Akay, B.N.; Argenziano, G.; Blum, A.; Braun, R.P.; Cabo, H.; Gourhant, J.Y.; Kreusch, J.; Lallas, A.; et al. Expert-Level Diagnosis of Nonpigmented Skin Cancer by Combined Convolutional Neural Networks. *JAMA Dermatol.* 2019, 155, 58–65. [CrossRef] [PubMed]
- 51. Dascalu, A.; David, E.O. Skin cancer detection by deep learning and sound analysis algorithms: A prospective clinical study of an elementary dermoscope. *EBioMedicine* **2019**, *43*, 107–113. [CrossRef]
- Pruneda, C.; Ramesh, M.; Hope, L.; Hope, R. Nonmelanoma Skin Cancers: Diagnostic Accuracy of Midlevel Providers vs. Dermatologists. Available online: https://www.hmpgloballearningnetwork.com/site/thederm/feature-story/nonmelanoma-skincancers-diagnostic-accuracy-midlevel-providers-vs#:~:text=A%20total%20of%2011,959%20NMSCs,clinical%20diagnosis%20 (Table%201) (accessed on 12 April 2023).
- Ho, C.J.; Calderon-Delgado, M.; Chan, C.C.; Lin, M.Y.; Tjiu, J.W.; Huang, S.L.; Chen, H.H. Detecting mouse squamous cell carcinoma from submicron full-field optical coherence tomography images by deep learning. *J. Biophotonics* 2021, 14, e202000271. [CrossRef]
- Huynh, T.; Nibali, A.; He, Z. Semi-supervised learning for medical image classification using imbalanced training data. Comput. Methods Programs Biomed. 2022, 216, 106628. [CrossRef] [PubMed]

- 55. Rezk, E.; Eltorki, M.; El-Dakhakhni, W. Leveraging Artificial Intelligence to Improve the Diversity of Dermatological Skin Color Pathology: Protocol for an Algorithm Development and Validation Study. *JMIR Res. Protoc.* **2022**, *11*, e34896. [CrossRef] [PubMed]
- 56. Daneshjou, R.; Vodrahalli, K.; Novoa, R.A.; Jenkins, M.; Liang, W.; Rotemberg, V.; Ko, J.; Swetter, S.M.; Bailey, E.E.; Gevaert, O.; et al. Disparities in dermatology AI performance on a diverse, curated clinical image set. *Sci. Adv.* **2022**, *8*, eabq6147. [CrossRef] [PubMed]

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