Received: 3 September 2022 | Revised: 14 November 2022 | Accepted: 1 December 2022

DOI: 10.1111/jocd.15565

JCD Journal of Cosmetic Dermatology WILEY

REVIEW ARTICLE

Artificial intelligence in Dermatopathology

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Abstract

Introduction: Ever evolving research in medical field has reached an exciting stage with advent of newer technologies. With the introduction of digital microscopy, pathology has transitioned to become more digitally oriented speciality. The potential of artificial intelligence (AI) in dermatopathology is to aid the diagnosis, and it requires dermatopathologists' guidance for efficient functioning of artificial intelligence.

Method: Comprehensive literature search was performed using electronic online databases "PubMed" and "Google Scholar." Articles published in English language were considered for the review.

Results: Convolutional neural network, a type of deep neural network, is considered as an ideal tool in image recognition, processing, classification, and segmentation. Implementation of AI in tumor pathology is involved in the diagnosis, grading, staging, and prognostic prediction as well as in identification of genetic or pathological features. In this review, we attempt to discuss the use of AI in dermatopathology, the attitude of patients and clinicians, its challenges, limitation, and potential opportunities in future implementation.

KEYWORDS
artificial intelligence, Dermatopathology, technology

1 | INTRODUCTION

Ever evolving medical research has reached an exciting stage with advent of new technologies which range from virtual reality, genetic analysis, stem cell therapy, and robotics to artificial intelligence (AI). With the invention of newer technologies, our approach to a dermatological condition, in terms of diagnosis or management, is rapidly evolving. Dermatology being a visually oriented speciality has taken a pivotal position in AI implementation, because of its large clinico-dermoscopic-histopathological image database. With the rapid development of digital microscopy, which facilitates digitalization of histopathological slides and with the advent of whole slide imaging (WSI), pathology has recently transitioned to become more digitally oriented medical speciality. Currently, the potential of use of AI in dermatopathology is to mainly complement the diagnosis. Guidance of dermatopathologist is enormous in training and efficient development of AI algorithms. Accumulation of large number of digital images represents an essential resource not only for education and research but also for efficient training of AI algorithms to improve workflow efficiency of a dermatopathologist. Several studies have evaluated the role of AI in dermatology.[1] Schaumberg[2] et al presented a machine learning method for disease prediction and immunostaining using thousands of images obtained from various articles. The use of AI in dermatopathology is considered as one of the most important and potential dermatological applications of AI.[3] Dermatopathologists play an important role, as their guidance is essential for training and development of AI algorithms. Hence, it is equally essential to know about the attitude of dermatopathologists toward the rapid increase in the use of AI in this field. In this review, we provide an overview about use of AI in dermatopathology, attitude of pathologists toward AI, its challenges and opportunities along with its future potential.

2 | AI IN DERMATOPATHOLOGY

Machine learning, a subset of AI, is the study of algorithms and data programming instructions that the computer learns automatically and utilizes to perform a task.[4] These machine learning methods can be supervised or unsupervised, based on whether the input data are fed with or without defined answer, respectively.[5] These methods are constrained by the amount of data available for learning. Reinforcement learning helps to maximize data analysis, so that the system learns from the environment in addition to the input data.[4] Neural networks are the most popular technique of machine learning, and the two popular subtypes of it are deep learning and convolutional neural networks (CNN).[6,7] Deep learning is a type of machine learning that utilizes artificial neural networks. These neural networks are mathematical models that use algorithms comprising of input, hidden and output layers. In simple neural networks, the intermediate or the hidden layer is only one but with the emerging computational power, it is possible to increase the hidden intermediate layer of the neural network infinitely to obtain more sensitive and a specific output. This multilayered neural network is involved in deep learning.[4] CNN is a type of artificial neural network that is primarily useful in image recognition, processing, classification, and segmentation. CNN is a deep neural network that is considered as an ideal tool in dermatopathological image analysis. Here, an image is disintegrated into a collection of pixels for effective image analysis. The three layers in CNN are convolutional layer, which forms fundamental component of the architecture performing extraction of the image, where each node is assigned a specific feature like color, shape, and size.[8] Then, the pooling layer classifies the input images by enabling CNN to accept inputs of different sizes and reduces the number of parameters to be studied. Then, finally the fully connected layer is involved in displaying the accurate output as per the input. A subclass of CNN known as region based CNN is involved in identification of a particular object within the image like location of the lesion.

3 | USE OF AI IN DIAGNOSTIC DERMATOPATHOLOGY

The concept of AI in dermatopathology was first described in 1987 with a system called TEGUMENT,[9] which was designed to identify about 986 histopathological diagnosis using light microscopic images with an accuracy of 91.8%. However, it required traditional medical source of information to be reorganized into the system. Hence, it was more of a computer aided human diagnosis than primarily a machine based analysis. However, with the advent of newer computational resources, direct machine based image analysis can now be a reality.[10]

4 | AI IN THE DIAGNOSIS OF MELANOCYTIC NEOPLASM

Melanoma is one of the primary causes of skin cancer related mortality, worldwide.[11] Like other cancers, it is primarily diagnosed by tissue biopsy. The emphasis on digital WSI is to augment the pathologist's intelligence that cannot be gleaned by manual examination. The most important role of AI is to distinguish malignant and benign pigmented lesions as the approach to treatment varies significantly based on the classification. In a study, Hekler[12] et al. used a total of 695 melanocytic neoplasms and classified them into nevus or melanoma. All stages of melanoma and the entire spectrum of nevi were represented. The digital images obtained were scanned, fragmented, segmented, and analyzed using the image database of CNN. In this study, CNN significantly outperformed ($p = 0.016$) pathologists in the accurate diagnosis of nevi and melanoma. The diagnostic discordance between dermatopathologists and AI was 20% for nevi, 18% for melanoma, and overall it was 19% but the discordance among dermatopathologists was around 25%–26%. A study by Logu FD et al.[13] developed an AI to recognize histopathological images of cutaneous melanoma. Here, 791 patches of normal skin and 1122 patches of pathological tissue were used for testing the diagnostic accuracy, sensitivity, and specificity of CNN and compared it with diagnostic accuracy by expert dermatologists as a reference. The results showed a high diagnostic accuracy of 96.5%, sensitivity of 95.7%, and specificity of 97.7% and concluded that deep learning system trained to recognize melanoma achieve higher accuracy compared to expert diagnosis. Deep learning is also been used in predilection of recurrence rate of distant metastasis and also disease specific survival rate in early melanoma. In a retrospective study, Kulkarni et al.[14] used scanned histopathological slides from 108 patients, and the images were divided into pixels, grids, and sequences, to be processed by CNN to obtain an accurate output. The output was further processed by recurrent neural network, which included region based CNN to obtain reginal information to predict the risk of recurrence or distant metastasis. Training was done using binary classification with positivity or negativity for metastatic recurrence. Both the testing sets showed a significant correlation for distant metastatic recurrence and also predicted disease specific survival as per Kaplan–Meier analysis ($p < 0.0001$). This model helps dermatopathologists to identify aggressive tumor and predict their success of treatment and survival with available treatment options. Brinker et al.[7] utilized 84 biopsy-proven dermoscopic images of melanoma and nevi and compared the assessment and recommended treatment between CNN and expert dermatologists in terms of overall accuracy, sensitivity, and specificity. The results showed a higher sensitivity (82.3%—CNN and 67.2%—expert dermatologists) and specificity (77.9%—CNN and 62.2%—expert dermatologists) with significant higher diagnostic accuracy for the AI algorithms ($p < 0.001$). Xie at al.[18] used 2241 histopathological images to classify melanoma and nevi and achieved high sensitivity (92%) and specificity (94%) in accurately distinguishing melanoma from nevi.

5 | AI IN THE DIAGNOSIS OF NON-MELANOCYTIC NEOPLASMS

In a study done by Olsen et al,[15] three individual AI algorithms were developed and trained to identify the WSI of seborrheic keratosis, dermal nevus, and nodular basal cell carcinoma. The WSI were broken down into pixels, and each pixel was used to train the CNN based on color contrast of the images. Compared to expert dermatopathologists, this binary classification was able to accurately diagnose seborrheic keratosis in 100%, dermal nevus in 99.3%, and nodular basal cell carcinoma in 99.45%. This study emphasized the potential of AI algorithms to improve diagnostic workflow of dermatopathologists. In order to obtain a real-world workflow, Ianni[16] et al created a deep learning algorithm to classify histopathological ESI into four categories, namely basaloid, melanocytic, squamoid, and others. This AI system in dermatopathology classified WSI into these 4 classes with an accuracy of 78%. Though this classifies the images into only these 4 categories, this algorithm can be used for diagnosis of common real world WSI including artifacts, poorly stained or prepared slides. Jiang et al.[17] used smartphones captured images and compared it with WSI in the diagnosis and classification of basal cell carcinoma (BCC) and inferred that AI can accurately diagnose BCC even when training is done with smartphone captured images. This emphasizes the potential of use of AI even in areas with limited resources but with higher occurrence of skin cancers. Fujisawa et al.[19] developed an AI algorithm for efficient classification of skin cancers using clinico-dermoscopic images of about 14 benign and malignant skin neoplasms and compared its accuracy with 13 expert dermatologists. The diagnostic accuracy was 76.5% with 96.3% sensitivity and a specificity of 89.5%, and the accuracy was significantly greater (92.4%) as compared to the diagnosis by expert dermatologist (85.3%). A recent study, done by Tschandl et al.[20], used clinical and dermoscopic images of non-pigmented lesions and compared the classification of CNN with 95 human experts (62 of which were board certified dermatologists). The CNN had higher accuracy than the experts in diagnosis and classification of common non-pigmented tumors like SCC, BCC, actinic keratosis, and keratoacanthoma but it was not as accurate for rare non-pigmented tumors like amelanotic melanoma. This study emphasized the role of adequacy of input data and how it can influence the final output if there is paucity of images in training CNN. A systematic review by Marka et al.[21] on 39 studies for detection of NMSC found that in most studies AI performed better in accurate diagnosis of NMSC in comparison with dermatologists. Cho et al.[22] showed that CNN performed on par with dermatologists and even outperformed dermatopathologists in diagnosis of malignant lesions of the lip. Roa et al[23] used a deep learning algorithm, to differentiate normal tissue from BCC using 1417 histopathological images and compared it with traditional approaches and showed that deep learning is superior to traditional approach with 91.4% accuracy.

6 | ATTITUDE TOWARD AI IN DERMATOPATHOLOGY

A survey by Polesie S et al.[24] on attitude of dermatopathologists toward AI showed an optimistic attitude about the impact and potential benefit of AI in dermatopathology. However, there is a strong need for education about AI and its potential benefits in dermatopathology.

A survey by Jutzi TB et al.[25] evaluated the attitude of patients toward AI in melanoma diagnostics. The results exhibited a positive attitude toward use of AI. However, patients were also concerned about data protection, possibility of errors, and impersonality. In addition, they expected a faster, more precise and unbiased diagnosis and less support from physicians.

AI may also be useful in dermatopathology research and in education for visual diagnosis and diagnostic reporting.

7 | LIMITATIONS

Although promising, current CNN models in dermatopathology have a narrow classification. Dermatopathologists are capable of recognizing various morphological variants of diseases and also can exclude wide number of differential diagnosis but most CNN can only identify if the image is positive/negative for a diagnosis.[26]

Due to the potential of high inter-observer-variability among dermatopathologists, it is difficult to develop and accurately train CNN which is in par with dermatopathologist in classifying various skin lesions.

At present, the data of images for various dermatosis are insufficient; also, the degree of image sharing among sources is poor and the quality of images is not uniform. For effective functioning of deep learning algorithms, there is a need for substantial quantity of diverse and high quality data to improve diagnostic efficacy. Though AI is known to improve efficiency of dermatopathologists, it is not feasible in resource-poor setting. There is an essential need for multidisciplinary involvement for accurate and efficient functioning of AI. Legal, ethical, and data privacy issues also need to be sorted out. Moreover, the complete humanistic or holistic approach cannot be achieved by AI.

8 | CHALLENGES FOR USE OF AI IN DERMATOPATHOLOGY

As histopathologic scans comprise of millions of pixels and are of higher dimensions, there are lot of technical challenges like lack of labeled data, the types of tissues could be infinite, the need for high quality extraction ultimately leads to higher computational expenses. Only histopathologic images based on deep learning algorithms may not perform better than dermatologists who have access to patient's medical history and clinical information.

Inter-class similarities and intra-class dissimilarities can lead to diagnostic challenges as deep learning algorithms need extensive training to reliably distinguish these lesions. There is a communication barrier between AI and dermatologists making it hard to interpret the decisions made by deep learning algorithms.[27]

9 | OPPORTUNITIES FOR IMPROVING PERFORMANCE OF AI

We are in an exciting time of AI with researchers claiming their systems outperforming dermatologists. However, the real life diagnostic are still performed by clinicians in diagnosing dermatological disorders especially skin cancers. In spite of these drawbacks, deep learning algorithms can perform very well in future especially with respect to diagnosing skin cancers.[27]

Other opportunities include creating balanced and diverse datasets and proper selection of cases and development of computer aided diagnosis which results in evolution of WSI in digital pathology, thus improving the performance of AI.[28,29]

Data augmentation with image transformations such as rotation, random crop, horizontal or vertical flip, shear, and translation may improve diagnostic accuracy. There is need for semantic explanation of the inferences obtained help in assisting the clinicians in their practice. Multiple deep learning algorithms help in evaluating different aspects of the lesions and generate a final conclusion. Additionally, multimodality solution and combination of clinical data and imaging features need to be incorporated to develop fusion data algorithms to provide accurate final prediction[31].

10 | CONCLUSION

With introduction of WSI and newer computational resources, AI in dermatopathology has gained a lot of attention during the recent years. AI is well trained in diagnosing melanoma, which is a binary simple classification. However, diagnosis of NMSC is difficult due to vast intra-class variability and interclass similarities. However, with further research and by incorporating the given opportunities, in future, AI can do very well not only for skin cancers but also for other dermatoses. Finally, it is very essential for dermatologists and pathologists to welcome AI and to realize that AI has the potential to support clinicians positively and will be dependent on clinicians for its efficient functioning and can never replace them.

AUTHOR CONTRIBUTIONS

Shishira R Jartarkar involved in writing and revising the manuscript. **Clay J Cockerell, Stephan Grabbe, Mahsa Babaei, Beate Weidenthaler-Barth, Martin Kassir, and Anant Patil involved in** review and revising the manuscript. **Mohamad Goldust involved in** conception, writing, review and revising the manuscript.

ACKNOWLEDGMENT

Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICAL APPROVAL

The authors declare that human ethics approval is not needed for this study

DISCLAIMER

"We confirm that the manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met and that each author believes that the manuscript represents honest work".

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How to cite this article: Jartarkar SR, Cockerell CJ, Patil A, et al. Artificial intelligence in Dermatopathology. *J Cosmet Dermatol*. 2023;22:1163-1167. doi:10.1111/jocd.15565