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Artificial Intelligence and Malignant Melanoma: A Review

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ABSTRACT

Malignant Melanoma is the most deadly form of skin cancer and one of the most quickly expanding cancers in the world. Some of melanocytic nevi have a higher risk of developing malignant melanoma. Early diagnosis of melanoma is critical due to increasing survival rates, decreasing surgical removal and following disfigurement, and reducing the overall care costs. Although the golden standard is histopathologic examination of the excised suspicious lesion, there are a number of tools which allow a more detailed examination of the skin lesion.

Artificial intelligence (AI) with its subfields (deep learning and machine learning) and imaging technologies have been incorporated in science and medicine. In dermatology, the rising incidence of melanoma, the benefits of early diagnosis, and the limited access to dermatologic services in some countries, have conduced developing of image-based, automated diagnostic systems and the usage of either clinical or dermoscopic images.

This article tries to overlook the studies in this field and give a general view of it.

Introduction

Malignant Melanoma is the most deadly form of skin cancer and one of the most quickly expanding cancers in the world.It often spreads to nearby lymph nodes, lungs, and brain. A melanocytic nevus (a nevocytic nevus or a mole) is a lesion containing nevus cells (a type of pigment cells called melanocytes) and some of them have a higher risk of developing malignant melanoma.There are various types of melanoma skin cancer such as nodular melanoma, superficial spreading melanoma, acral lentiginous, and lentigo maligna.

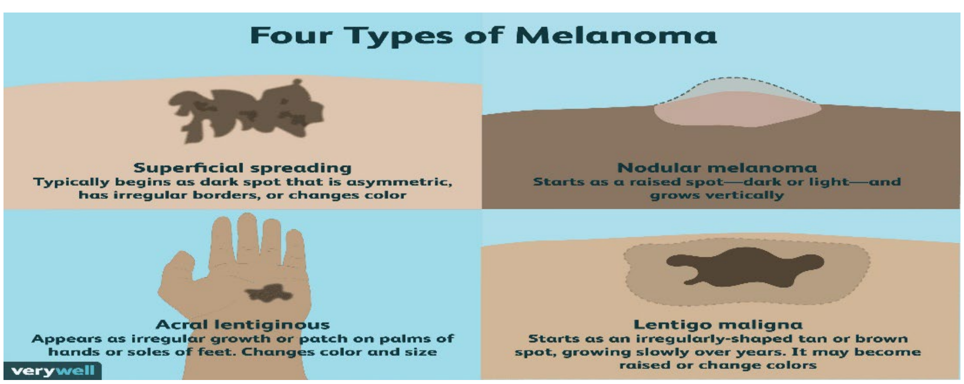

Figure 1. 4 types of Melanoma

Early diagnosis of melanoma is critical. Survival rates decrease extremely with increasing thickness.

For a suspicious pigmented skin lesion, there are several steps before a definitive diagnosis of melanoma: self-evaluation, evaluation by a primary care physician, assessment by a specialist, and excision and assessment by histopathology.

The detection of the disease starts with the visual examination of skin lesion by dermatologists but the golden standard is histopathologic examination of the excised suspicious lesion.

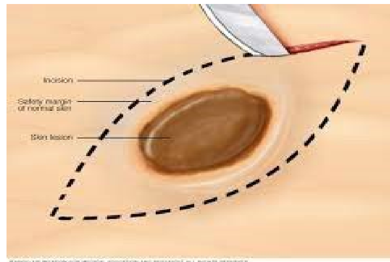

Figure 2. Biopsy of suspicious lesion. Excisional biopsy with 2 mm margins is the optimal method of biopsy for suspicious pigmented lesions.

"Two-Step Procedure" is the most common method for the diagnosis consists of 2 steps:

- Recognition of melanocytic lesion
- Calculation the degree of malignancy(staging)

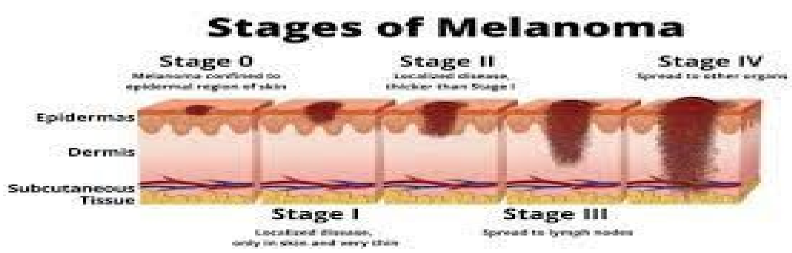

Figure 3. Stages of Melanoma. There are some factors describing the cancer: tumor thickness**,** ulceration**,** the spread to nearby lymph nodes, and metastasis to distant sites. As a rule, the lower the number, the less the cancer has spread.

There are a number of tools which allow a more detailed examination of the skin lesion, compared to examination by the naked eye alone.

Dermoscopy , the most widely employed technology, is a noninvasive technique which can enlarge skin images by nearly 10 times. It allows clinicians to visualize the epidermis, the boundary between the epidermis and dermis, and the upper layer of the dermis through the stratum corneum accurately. It works based on applying a light source and a transparent plate or mineral oil, alcohol, or water applied on a lesion.

Multicomponent pattern, irregular dots/globules, atypical pigment network, irregular streaks, irregular pigmentation, regression structures, and blue whitish veil are dermoscopic features describing melanoma.

Nevertheless, requiring much experience and time, being prone to error and subjective decisions are its drawbacks.

Spectroscopy, including fluorescence and Raman spectroscopy, is a technique which obtains information of cell characteristics by measuring electromagnetic waves passing through skin lesions.
Raman spectroscopy is on the basis of Raman effect caused by molecular vibrations according to the structure of the molecules. Raman spectrum is the presentation of the frequency shifts of scattered light from a sample irradiated with laser light. It is complex and its interpretation is subjective and time consuming.

Reflectance Confocal Microscopy (RCM) is non-invasive axial optical sectioning that shows microscopic features of normal skin. It is applied thoroughly for imaging benign and malignant lesions in vivo. RCM can access the epidermis and superficial dermis layers below the surface of the skin where melanomas arises. It can play the role of intermediary between visual inspection and biopsy.

Total Body Photography (TBP) is the imaging of different parts of the body. In 3D TBP, a matrix of cameras take photos at once covering the body from all angles. These can help clinicians to monitor nevi for change and marker of malignant transformation especially in patients with many nevi or a personal or family history of melanoma. But in 2D TBP, a series of anatomic postures by a single camera is captured. In both of them some areas such as at the soles of the feet, scalp, genitals, and other folds of the body can be missed.

Removal of every pigmented lesion especially in the case of multiple skin lesions or lesions localized in cosmetically important parts of the body such as the face has the risk of scarring.

Early detection is important for reducing:
-the size and extent of surgical removal which causes less disfigurement
-side effects of systemic therapies
-the overall care costs

Dermatologists are the best specialists to provide early detection, but the time of access to their services plays major role in early detection. Therefore, in some countries, the use of e-Health and tele-dermatology has increased because of lack of dermatologists over the last 10 years.

Artificial intelligence (AI) is a field of computer science which makes a computer system mimic human intelligence. Machine Learning (ML), as a subfield of AI, enables a computer system to make predictions or some decisions using historical data. Using these technologies, computers can be trained to accomplish specific tasks by processing large amounts of data and recognizing patterns in the data.
According to the data and the application, the algorithms used can be supervised (the algorithm is trained on human-labeled data) or unsupervised (the algorithm is trained on unlabeled data and will search for patterns by itself).

Deep learning, as a highly specialized artificial neural network subtype of ML, is significantly inspired by the way the human brain works. Convolutional layers and the overall architectural structure of deep learning systems make it notable classifiers of disease and feature extractors.

Artificial Intelligence and imaging technologies have been incorporated in science and medicine. CAD systems and their components, dedicated to skin lesion detection, were introduced at the beginning of 1990.A CAD system is an automatic tool used to support dermatologists in their diagnoses.Using artificial intelligence in the design of computer-aided diagnosis (CAD) has dramatically improved.

In dermatology, the rising incidence of melanoma, the benefits of early diagnosis, and the limited access to dermatologic services in some countries have conduced developing of image-based, automated diagnostic systems and the usage of either clinical or dermoscopic images.

A similar level of accuracy of melanoma detection by the algorithm and specialists was shown in study. Definitely, successful CAD would most probably enhance and support dermatologists rather than replace them.

Success of the AI application in “real life” clinical setting is associated with the consent of the physician and the patient. Most participants showed a positive attitude toward the use of artificial intelligence as an assistance system in melanoma diagnostics. Although their concerns and questions (biases, safety, privacy and ethics) should be addressed suitably.

Deep learning and machine learning are both subfields of artificial intelligence which learn from data without being explicitly programmed. These framework achieve a specific task or answer a specific question using proper algorithms and valid data. AI and its subtypes, in contrast to traditional computer programming, make more robust predictive programs and reproduce the decision of the dermatologist based on images.

3-1-Design of a computer-aided diagnosis system consists of several main stages: data (including imagining and non-visual data) acquisition, preprocessing, segmentation, feature extraction and selection, classification, and evaluation.

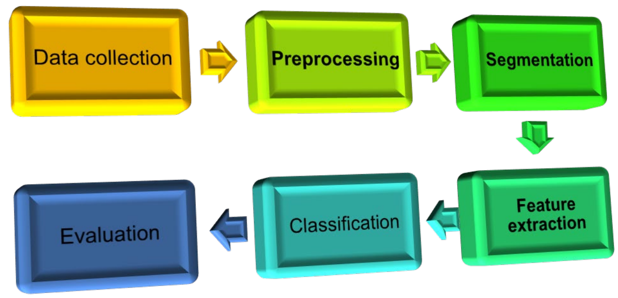

Figure 4. Sequential steps of Automated Image Analysis System

There are several sources of images for the systems:

- HAM10000 is the latest publicly available skin lesions dataset, containing 10,015 dermoscopic images in all important diagnostic categories in the realm of pigmented lesions.

- PH² Contains 200 dermoscopic images which were acquired using a Tuebinger-Mole-Analyzer system at the Dermatology Center of Pedro Hispano Hospital, Portugal. It was divided into 80 images of common nevi, 80 images of atypical nevi, and 40 images of melanoma skin cancers which were visually inspected and manually annotated by an expert dermatologist according to dermoscopic criteria of streaks, colors, regression areas, pigment network, and blue-whitish veil globules.

- ISIC Archive The ISIC archive, a collection of various skin lesions datasets, was originally released by the International Skin Imaging Collaboration at the International Symposium on Biomedical Imaging (ISBI) Challenge 2016 (ISIC2016). The ISIC2016 archive consists of two subsets: training (900 images) and testing (379 images). Its images include two classes: malignant melanomas (30.3%) and benign nevi (69.7%).
In the ISIC2017 dataset, a category of Seborrheic-keratoses (SK) images was added. The dataset contains 2000 training images including 150 validation images and 600 images for testing.
The ISIC2019 dataset contains 25,331 images of eight different categories of skin lesions such as melanoma, melanocytic-nevus, BCC, AK, benign keratosis, dermatofibroma, vascular lesion, and SCC. It also includes metadata for images such as sex, age, and area of the patient.

- Atlas Derm The Atlas of Dermoscopy dataset is a combination of a book and images on CD-ROM with various cases of skin lesions and corresponding dermoscopic images for every case. It was provided by two university hospitals (University of Naples, Italy; and University of Graz, Austria).

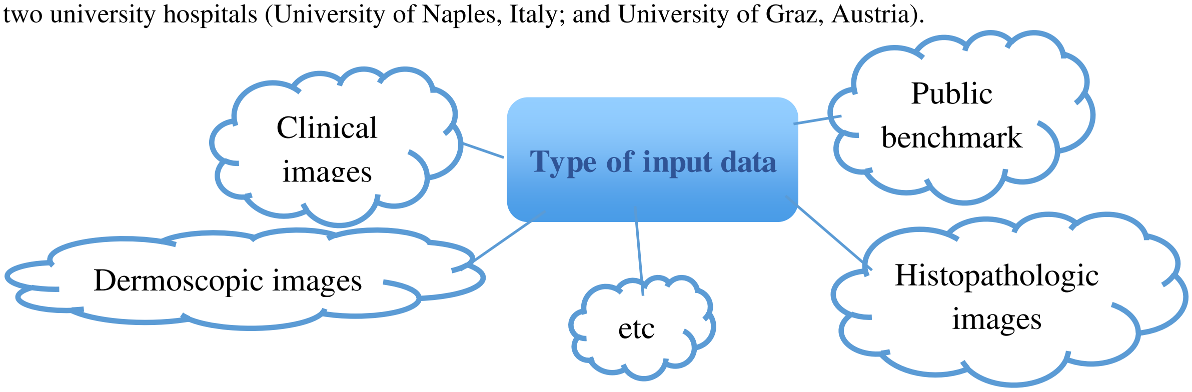

Figure 5. Sources of images used in CAD systems.

Preprocessing is an essential part of the system because dermoscopic images contain artifacts which make the next stages impossible. There are several techniques for enhancing images and reducing the amount of artifacts and noise. Black frame removal, smoothing of the air bubbles, black hair removal, inpainting, noise removal, contrast enhancement, filtering, and resizing are preprocessing techniques used for removing or even reducing the unrelated and surplus parts in the dermoscopic images.

Segmentation of the lesion from the background skin - the fundamental and outstanding step to analyze images - identifies the location of the lesion border and makes the lesion's shape and color identifiable and comparable with the color of the surrounding skin.

There are several factors making segmentation extremely difficult for dermoscopic images : low contrast between the healthy skin and moles, irregular borders, misleading factors such as hair, markers, bad frames, size, blood vessels, and air bubbles.

Some segmentation techniques such as region-based segmentation, watershed segmentation, level set segmentation, texture-based segmentation, histogram thresholding-based segmentation, clustering-based segmentation, edge-based segmentation, morphological segmentation, model-based segmentation, soft computing segmentation, and active contour segmentation are used.

Feature extraction - the crucial and important step after segmentation - is about deriving information from the original features set. It detects and localizes an image to decrease redundant data and improves the relevant information.

The segmented image is usually used as the input to feature extraction. Hand-crafted or automatically extracted features can be used for melanoma detection according to the segmentation results.

ACDs based on AI use a series of lesion characteristics learned from analyzing thousands of other images for comparing and assessing the likelihood of melanoma.

Due to commonly accepted protocols for skin cancer detection, ABCD Rule, 7-point Checklist, Pattern Analysis, Menzies Method, Revised Pattern Analysis, 3-point Checklist, 4-point Checklist, and CASH Algorithm, most of CAD systems use machine learning to create a model using different mathematical equations based on observed features. Intensity, geometrical, morphological, fractal dimension based, and texture features are utilized for the analysis of medical images.

Concerning melanoma, there are different quantitative metrics which are high for melanoma and low for other lesions such as irregularity and asymmetry, aspect ratio and maximum diameter, border, brightness, colors(blue , blue-black color), organization of pigmented network pattern(reticular pattern), blue-white veil, streaks, globules, dots, and structural components present in the lesion(blotches or regression structures).

Feature selection is about selecting a subset of features out of the original features. It reduces model complexity, increases prediction accuracy and enhances the computational efficiency by rejecting redundant, unimportant, or noisy features.

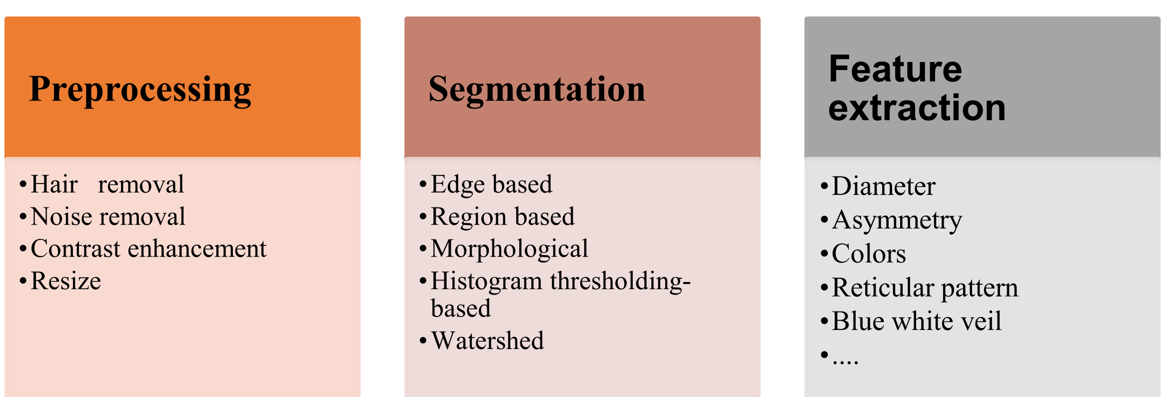

Figure 6. Techniques and lesion characteristics used for feature selection

Classification is the process of predicting the class of given data points. Many algorithms are used to calculate a set of values derived by previous steps. This process describes the lesion by a number of characteristics according to the aim of plan.

Classic deep learning techniques for skin cancer detection :

- Artificial Neural Networks (ANN) is a nonlinear and statistical prediction method including three layers of neurons: input layer, second/intermediate or hidden layer, and the third layer of output neurons. The number of hidden layers in an ANN depends on the number of input images. the complex associations/relationships between input and output layers are learned at each layer using back-propagation. According to using a supervised or unsupervised learning mechanism, The dataset can be labeled or unlabeled. After training/classification of the training set, input images are classified as melanoma or non-melanoma.

- Convolutional Neural Networks (CNN) is an essential type of deep neural network, which consists of several convolutional layers (involving linear and nonlinear operators), is used for classifying images, assembling a group of input images, and performing image recognition tasks. It learns by collecting more straight features to afford complex features. Convolution layers, pooling layers, and full-connected layers are major types of layers making CNN.

- Kohonen Self-organizing Neural Networks (KNN) is a very famous type of deep neural network. It is trained on the basis of unsupervised learning and consists of two layers: input layer and competitive layer. It can be used for data clustering without knowing the relationships between input data members. It preserves the topological structure of the input data space during mapping dimensionality from high to low.

- Generative Adversarial Neural Networks (GAN) is a powerful class of DNN that is composed of 2 neural networks such as a generator and a discriminator which compete with each other to analyze and capture the variance in a database.

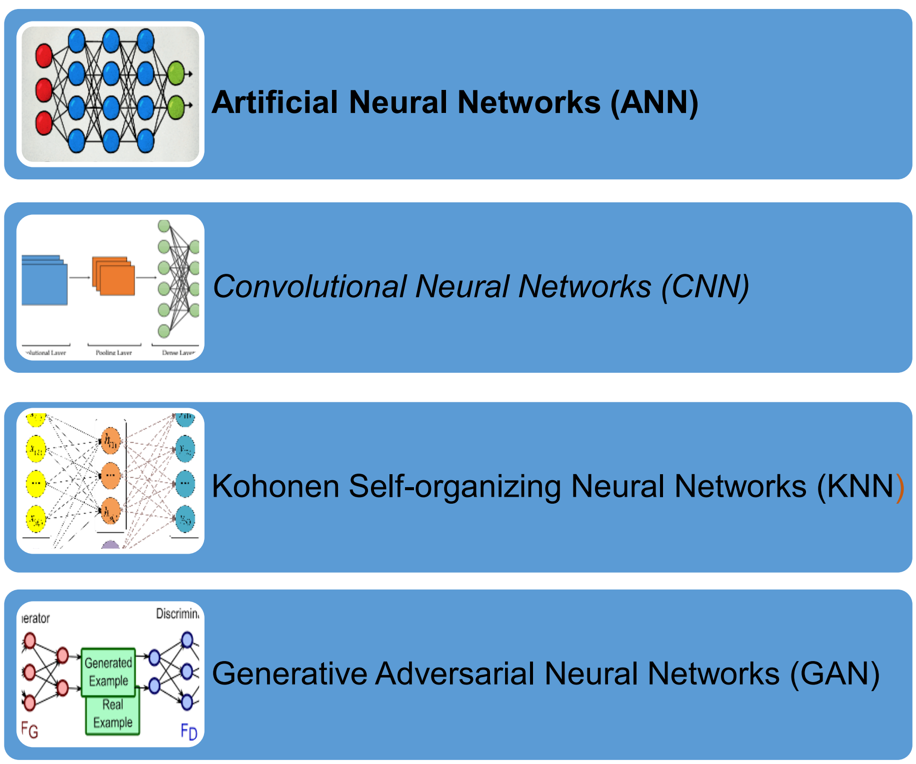

Figure 7. Classic deep learning techniques for classification

Due to advantages and disadvantages of each algorithm, the best results depends on the proper selection of technique. CNN, because of its close relations to computer vision, is more suitable for image analysis.

Evaluation is the way to explain the performance and robustness of a model. There are different evaluation metrics according to the type of model and the implementation plan of the model.

Skin cancer detection is mostly evaluated by the following metrics:

- Accuracy is the proportion of the total number of predictions that were correct .It indicates the percent ratio between the total number of correctly classified lesions and the overall number of examined lesions.
- Sensitivity or Recall is the proportion of actual positive cases which are correctly identified .It is the percent ratio between cases that are correctly assigned as positive in comparison with the overall number of positive cases contained in the data set.
- Specificity is the proportion of actual negative cases which are correctly identified. It is the percent ratio between cases correctly allocated as negative and all negative cases of the data set.
- ROC (The Receiver Operating Characteristic) curve is a plot between the true positive rate (y-axis) against the false positive rate (x-axis). The Area Under the Curve (AUC) is the measure of the ability of a classifier to distinguish between classes and is used as a summary of the ROC curve.

Material and Method

For this review, I searched through the PubMed database. PubMed was screened for studies published in English between 2000-2021. The key words were“ AI and melanoma detection”. Search results were screened manually and at first, the titles were read then the abstracts. Articles were selected if they had used AI for screening or diagnosis of melanoma or its contributions were noted in these fields. Studies concentrating on prognosis, therapy, and other skin cancers were excluded. This part was done under observation of a general practitioner.

Results and Discussion

At first, I found 94 article, after the first screening I chose 67 articles which, their titles and abstracts would match to the aim of review. In this part, I read all of them and took notes about the aim of the study, introduction, methods, datasets, tools, and results including strengths and limitations. According to this part, some articles were excluded due to their results and full text unavailability. At last I collected 53 papers for final screening.

According to results, the first publications date back to 2004. Most papers were published between 2016 to 2021 and the peak was in 2020 (11 publications), 2021, and 2019 (10-9 publications). 39 studies proposed and presented a CAD or a part of it for early detection of melanoma, however, other 15 studies proceeded to survey in other aspects of AI in melanoma detection.

All of the studies had an introduction about skin cancer focusing on malignant melanoma and had some brief explanations about AI and its participation in new medical world. The ISIC was mostly used as data set and later the Interactive Atlas of Dermatology and PH². Indubitably, many studies used dermoscopic/clinical images for their research. It seems that generating new data set using apps, especially prospective image data, can improve the accuracy of artificial intelligence frameworks.

The biggest size of data collection was 17,302 images from the ISIC 2019 , the largest public skin lesion image dataset, and the smallest number of images were 22. Almost all studies selected data sets divided in training, testing and/or validation set and the biggest percentage(more than 60%) belonged to training set except one study ,which allocated 50% of the total image dataset to each set (training and testing data sets).

There are some limitations in applying any CAD for melanoma detection. The small size of data sets or samples is the biggest one. It can also cause some additional problems. Unbalanced datasets (When the distribution of examples across the known classes is biased or skewed) and overfitting (when function corresponds too closely to a particular set of data) can occur in small size data sets and can lead to the decrease of generalizability (the ability of a model to predict accurately on varied data sources not included in the model's training dataset) and affect the sensitivity. Naturally, noisy images can lead to overfitting .To overcome these difficulties, many studies used techniques such as using data validation, regularization and augmentation.

Lack of some relevant factors such as age, sex, skin color, various genetic risk factors for melanoma, patient demographics, racial, ethnic, and socioeconomic backgrounds, size, site and history of lesion especially less common presentations and all anatomic sites are important and challenging.

Other limitations which the studies noted are dependent on training of the users, high yield of melanoma due to conducting in specialized referral centers, using images of images, internet access, and resistance of patients to AI tools. Since most of the frameworks designed in studies were binary classes (Melanoma /Non-melanoma or Benign lesion - Melanoma / Nevi – requiring excision / not requiring excision), their results were presented based on accuracy or ROCAUR, sensitivity and specificity. The highest ACC was 99% for an automated segmentation method using the U-Net and the ResNet architectures, and 98% for artificial neural networks (ANNs) comparatively with convolution neural networks. The least accuracy was 72.10% based on the verification set. Area under the ROC curve was 78.4% for Fuzzy logic techniques in Relative color blotches and 97% for a combination of CNN for image data combined with an artificial neural network (ANN) for patient's metadata (CNN+ANN model).

Two studies reached 100% using the Deep Ensemble foe Recognition of Malignancy and 98% sensitivity for an automated approach generating imaging biomarkers.The lowest sensitivity was 67.5% for a cad extracting specific classification parameters.The lowest specificity was 36% for screening algorithms using imaging biomarkers of hyperspectral dermoscopy and an automated approach generating imaging biomarkers.The highest specificity ,99%, was reported in the first study of neural network analysis of Raman spectra for MM diagnosis.

In total, comparative studies have shown similar or higher performance of artificial algorithms. Attention to physician's and patient's perspectives on applying the AI tools in clinical real world should be considered. Although entrance of AI in the medical field has led to an increase of diagnostic speed and triage efficiency, decreasing of health care cost and patient anxiety, there are concerns about biases, safety, privacy of the patient and loss of the human physician-patient relationship.

Conclusion

Malignant melanoma is one of the most common types of cancer affecting humans. Traditional skin cancer diagnosis methods, in addition to being costly, require a professional physician and take a considerable amount of time. The potential of AI in clinical decision making support and image analysis has been demonstrated. Image recognition technology based on machine learning algorithms can classify skin cancers nearly as successfully as human experts.

Nowadays, especially after COVID-19 Pandemic, digital and computing systems have dramatically progressed. Opportunities for AI to benefit clinical researchers and the patients are steadily increasing .It is not unpredictable that AI will become an essential part of the digital healthcare systems that shape and support modern medical techniques. Therefore, it is wise to pay more attention to possible medical applications of AI. This review tried to collect and summarize the endeavors for detecting melanoma using AI at a simple readability to be used by new researchers for background reading. By using wider collections of original research papers and reviews from a various number of databases and literature search engines, more comprehensive reviews of the vastly growing field of AI for melanoma detection can be created. I hope that this review will be of use to those seeking to enter the flow of ongoing research in AI and malignant melanoma.

Limitations

This research faced a number of obstacles such as limited access to wider research papers and databases. In this way, a number of non-open access research papers and reviews could not be studied. Selecting finite keywords led to narrow publication search results. It is expected that using a variety of research publications (both from open access and non-open access resources) and more appropriate key words, this research topic can be studied thoroughly through different aspects.

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References

Sivaraj S, Malmathanraj R, Palanisamy P. Detecting anomalous growth of skin lesion using threshold-based segmentation algorithm and Fuzzy K-Nearest Neighbor classifier. J Cancer Res Ther. 2020 Jan-Mar;16(1):40-52. http://doi.org/10.4103/jcrt. JCRT_306_17. PMID: 32362608.

Jaworek-Korjakowska J, Kłeczek P. Automatic Classification of Specific Melanocytic Lesions Using Artificial Intelligence. *Biomed Res Int*. 2016;2016:8934242. http://doi.org/10.1155/2016/8934242

Dildar M, Akram S, Irfan M, et al. Skin Cancer Detection: A Review Using Deep Learning Techniques. *Int J Environ Res Public Health*. 2021;18(10):5479. Published 2021 May 20. http://doi.org/10.3390/ijerph18105479

Lee KJ, Janda M, Stark MS, Sturm RA, Soyer HP. On Naevi and Melanomas: Two Sides of the Same Coin?. *Front Med (Lausanne)*. 2021;8:635316. Published 2021 Feb 19. http://doi.org/10.3389/fmed.2021.635316

Phillips M, Marsden H, Jaffe W, Matin RN, Wali GN, Greenhalgh J, McGrath E, James R, Ladoyanni E, Bewley A, Argenziano G, Palamaras I. Assessment of Accuracy of an Artificial Intelligence Algorithm to Detect Melanoma in Images of Skin Lesions. JAMA Netw Open. 2019 Oct 2;2(10):e1913436. http://doi.org/10.1001/jamanetworkopen. 2019.13436. Erratum in: JAMA Netw Open. 2019 Nov 1;2(11):e1916430. PMID: 31617929; PMCID: PMC6806667.

Pham TC, Luong CM, Hoang VD, Doucet A. AI outperformed every dermatologist in dermoscopic melanoma diagnosis, using an optimized deep-CNN architecture with custom mini-batch logic and loss function. *Sci Rep*. 2021;11(1):17485. Published 2021 Sep 1. http://doi.org/10.1038/s41598-021-96707-8

García Arroyo JL, García Zapirain B. Detection of pigment network in dermoscopy images using supervised machine learning and structural analysis. Comput Biol Med. 2014 Jan;44:144-57. http://doi.org/10.1016/j.compbiomed. 2013.11.002. Epub 2013 Nov 12. PMID: 24314859.

Ferrante di Ruffano L, Takwoingi Y, Dinnes J, et al. Computer-assisted diagnosis techniques (dermoscopy and spectroscopy-based) for diagnosing skin cancer in adults. *Cochrane Database Syst Rev*. 2018;12(12):CD013186. Published 2018 Dec 4. http://doi.org/10.1002/14651858.CD013186

Gniadecka M, Philipsen PA, Sigurdsson S, Wessel S, Nielsen OF, Christensen DH, Hercogova J, Rossen K, Thomsen HK, Gniadecki R, Hansen LK, Wulf HC. Melanoma diagnosis by Raman spectroscopy and neural networks: structure alterations in proteins and lipids in intact cancer tissue. J Invest Dermatol. 2004 Feb;122(2):443-9. http://doi.org/10.1046/j.0022-202X. 2004.22208.x. PMID: 15009728.

Hosking AM, Coakley BJ, Chang D, et al. Hyperspectral imaging in automated digital dermoscopy screening for melanoma. *Lasers Surg Med*. 2019;51(3):214-222. doi:10.1002/lsm.23055

Stoecker WV, Gupta K, Stanley RJ, Moss RH, Shrestha B. Detection of asymmetric blotches (asymmetric structureless areas) in dermoscopy images of malignant melanoma using relative color. *Skin Res Technol*. 2005;11(3):179-184. http://doi.org/10.1111/j.1600-0846.2005.00117.x

Kim CI, Hwang SM, Park EB, Won CH, Lee JH. Computer-Aided Diagnosis Algorithm for Classification of Malignant Melanoma Using Deep Neural Networks. *Sensors (Basel)*. 2021;21(16):5551. Published 2021 Aug 18. http://doi.org/10.3390/s21165551

Öztürk Ş, Özkaya U. Skin Lesion Segmentation with Improved Convolutional Neural Network. *J Digit Imaging*. 2020;33(4):958-970. http://doi.org/10.1007/s10278-020-00343-z

Gareau D, Hennessy R, Wan E, Pellacani G, Jacques SL. Automated detection of malignant features in confocal microscopy on superficial spreading melanoma versus nevi. *J Biomed Opt*. 2010;15(6):061713. http://doi.org/10.1117/1.3524301

Kurugol S, Dy JG, Brooks DH, Rajadhyaksha M. Pilot study of semiautomated localization of the dermal/epidermal junction in reflectance confocal microscopy images of skin. *J Biomed Opt*. 2011;16(3):036005. http://doi.org/10.1117/1.3549740

Petrie T, Samatham R, Witkowski AM, Esteva A, Leachman SA. Melanoma Early Detection: Big Data, Bigger Picture. *J Invest Dermatol*. 2019;139(1):25-30. http://doi.org/10.1016/j.jid.2018.06.187

Giavina-Bianchi M, de Sousa RM, Paciello VZA, et al. Implementation of artificial intelligence algorithms for melanoma screening in a primary care setting. *PLoS One*. 2021;16(9):e0257006. Published 2021 Sep 22. http://doi.org/10.1371/journal.pone.0257006

Shields CL, Lally SE, Dalvin LA, et al. White Paper on Ophthalmic Imaging for Choroidal Nevus Identification and Transformation into Melanoma. *Transl Vis Sci Technol*. 2021;10(2):24. http://doi.org/10.1167/tvst.10.2.24

Dick V, Sinz C, Mittlböck M, Kittler H, Tschandl P. Accuracy of Computer-Aided Diagnosis of Melanoma: A Meta-analysis. *JAMA Dermatol*. 2019;155(11):1291-1299. http://doi.org/10.1001/jamadermatol.2019.1375

Jutzi TB, Krieghoff-Henning EI, Holland-Letz T, et al. Artificial Intelligence in Skin Cancer Diagnostics: The Patients' Perspective. *Front Med (Lausanne)*. 2020;7:233. Published 2020 Jun 2. http://doi.org/10.3389/fmed.2020.00233

Chuchu N, Takwoingi Y, Dinnes J, et al. Smartphone applications for triaging adults with skin lesions that are suspicious for melanoma. *Cochrane Database Syst Rev*. 2018;12(12):CD013192. Published 2018 Dec 4. http://doi.org/10.1002/14651858.CD013192

Zafar K, Gilani SO, Waris A, et al. Skin Lesion Segmentation from Dermoscopic Images Using Convolutional Neural Network. *Sensors (Basel)*. 2020;20(6):1601. Published 2020 Mar 13. http://doi.org/10.3390/s20061601

Erkol B, Moss RH, Stanley RJ, Stoecker WV, Hvatum E. Automatic lesion boundary detection in dermoscopy images using gradient vector flow snakes. *Skin Res Technol*. 2005;11(1):17-26. http://doi.org/10.1111/j.1600-0846.2005.00092.x

Jahanifar M, Zamani Tajeddin N, Mohammadzadeh Asl B, Gooya A. Supervised Saliency Map Driven Segmentation of Lesions in Dermoscopic Images. IEEE J Biomed Health Inform. 2019 Mar;23(2):509-518. http://doi.org/10.1109/JBHI.2018.2839647. Epub 2018 May 22. PMID: 29994323.

Li Y, Shen L. Skin Lesion Analysis towards Melanoma Detection Using Deep Learning Network. *Sensors (Basel)*. 2018;18(2):556. Published 2018 Feb 11. http://doi.org/10.3390/s18020556

Erol R, Bayraktar M, Kockara S, Kaya S, Halic T. Texture based skin lesion abruptness quantification to detect malignancy. *BMC Bioinformatics*. 2017;18(Suppl 14):484. Published 2017 Dec 28. http://doi.org/10.1186/s12859-017-1892-5

Jaworek-Korjakowska J. Computer-Aided Diagnosis of Micro-Malignant Melanoma Lesions Applying Support Vector Machines. *Biomed Res Int*. 2016;2016:4381972. http://doi.org/10.1155/2016/4381972

Lingala M, Stanley RJ, Rader RK, et al. Fuzzy logic color detection: Blue areas in melanoma dermoscopy images. *Comput Med Imaging Graph*. 2014;38(5):403-410. http://doi.org/10.1016/j.compmedimag.2014.03.007

Celebi ME, Iyatomi H, Stoecker WV, et al. Automatic detection of blue-white veil and related structures in dermoscopy images. *Comput Med Imaging Graph*. 2008;32(8):670-677. http://doi.org/10.1016/j.compmedimag.2008.08.003

Khan A, Gupta K, Stanley RJ, et al. Fuzzy logic techniques for blotch feature evaluation in dermoscopy images. *Comput Med Imaging Graph*. 2009;33(1):50-57. http://doi.org/10.1016/j.compmedimag.2008.10.001

Haggenmüller S, Maron RC, Hekler A, Utikal JS, Barata C, Barnhill RL, Beltraminelli H, Berking C, Betz-Stablein B, Blum A, Braun SA, Carr R, Combalia M, Fernandez-Figueras MT, Ferrara G, Fraitag S, French LE, Gellrich FF, Ghoreschi K, Goebeler M, Guitera P, Haenssle HA, Haferkamp S, Heinzerling L, Heppt MV, Hilke FJ, Hobelsberger S, Krahl D, Kutzner H, Lallas A, Liopyris K, Llamas-Velasco M, Malvehy J, Meier F, Müller CSL, Navarini AA, Navarrete-Dechent C, Perasole A, Poch G, Podlipnik S, Requena L, Rotemberg VM, Saggini A, Sangueza OP, Santonja C, Schadendorf D, Schilling B, Schlaak M, Schlager JG, Sergon M, Sondermann W, Soyer HP, Starz H, Stolz W, Vale E, Weyers W, Zink A, Krieghoff-Henning E, Kather JN, von Kalle C, Lipka DB, Fröhling S, Hauschild A, Kittler H, Brinker TJ. Skin cancer classification via convolutional neural networks: systematic review of studies involving human experts. Eur J Cancer. 2021 Oct;156:202-216. http://doi.org/10.1016/j.ejca.2021.06.049. Epub 2021 Sep 8. PMID: 34509059.

Marchetti MA, Codella NCF, Dusza SW, et al. Results of the 2016 International Skin Imaging Collaboration International Symposium on Biomedical Imaging challenge: Comparison of the accuracy of computer algorithms to dermatologists for the diagnosis of melanoma from dermoscopic images. *J Am Acad Dermatol*. 2018;78(2):270-277.e1. http://doi.org/10.1016/j.jaad.2017.08.016

Ningrum DNA, Yuan SP, Kung WM, et al. Deep Learning Classifier with Patient's Metadata of Dermoscopic Images in Malignant Melanoma Detection. *J Multidiscip Healthc*. 2021;14:877-885. Published 2021 Apr 21. http://doi.org/10.2147/JMDH.S306284

Maron RC, Utikal JS, Hekler A, et al. Artificial Intelligence and Its Effect on Dermatologists' Accuracy in Dermoscopic Melanoma Image Classification: Web-Based Survey Study. *J Med Internet Res*. 2020;22(9):e18091. Published 2020 Sep 11. http://doi.org/10.2196/18091

Alsaade FW, Aldhyani THH, Al-Adhaileh MH. Developing a Recognition System for Diagnosing Melanoma Skin Lesions Using Artificial Intelligence Algorithms. *Comput Math Methods Med*. 2021;2021:9998379. Published 2021 May 15. http://doi1.org/0.1155/2021/9998379

Haenssle HA, Fink C, Schneiderbauer R, Toberer F, Buhl T, Blum A, Kalloo A, Hassen ABH, Thomas L, Enk A, Uhlmann L; Reader study level-I and level-II Groups, Alt C, Arenbergerova M, Bakos R, Baltzer A, Bertlich I, Blum A, Bokor-Billmann T, Bowling J, Braghiroli N, Braun R, Buder-Bakhaya K, Buhl T, Cabo H, Cabrijan L, Cevic N, Classen A, Deltgen D, Fink C, Georgieva I, Hakim-Meibodi LE, Hanner S, Hartmann F, Hartmann J, Haus G, Hoxha E, Karls R, Koga H, Kreusch J, Lallas A, Majenka P, Marghoob A, Massone C, Mekokishvili L, Mestel D, Meyer V, Neuberger A, Nielsen K, Oliviero M, Pampena R, Paoli J, Pawlik E, Rao B, Rendon A, Russo T, Sadek A, Samhaber K, Schneiderbauer R, Schweizer A, Toberer F, Trennheuser L, Vlahova L, Wald A, Winkler J, Wölbing P, Zalaudek I. Man against machine: diagnostic performance of a deep learning convolutional neural network for dermoscopic melanoma recognition in comparison to 58 dermatologists. Ann Oncol. 2018 Aug 1;29(8):1836-1842. http://doi.org/10.1093/annonc/mdy166. PMID: 29846502

Gareau DS, Browning J, Correa Da Rosa J, et al. Deep learning-level melanoma detection by interpretable machine learning and imaging biomarker cues. *J Biomed Opt*. 2020;25(11):112906. http://doi.org/10.1117/1.JBO.25.11.112906

Marchetti MA, Liopyris K, Dusza SW, et al. Computer algorithms show potential for improving dermatologists' accuracy to diagnose cutaneous melanoma: Results of the International Skin Imaging Collaboration 2017. *J Am Acad Dermatol*. 2020;82(3):622-627. http://doi.org/10.1016/j.jaad.2019.07.016

Yu C, Yang S, Kim W, et al. Acral melanoma detection using a convolutional neural network for dermoscopy images [published correction appears in PLoS One. 2018 Apr 24;13(4):e0196621]. *PLoS One*. 2018;13(3):e0193321. Published 2018 Mar 7. http://doi.org/10.1371/journal.pone.0193321

Nasiri S, Helsper J, Jung M, Fathi M. DePicT Melanoma Deep-CLASS: a deep convolutional neural networks approach to classify skin lesion images. *BMC Bioinformatics*. 2020;21(Suppl 2):84. Published 2020 Mar 11. http://doi.org/10.1186/s12859-020-3351-y

Gilmore SJ. Automated decision support in melanocytic lesion management. *PLoS One*. 2018;13(9):e0203459. Published 2018 Sep 7. http://doi.org/10.1371/journal.pone.0203459

Połap D, Winnicka A, Serwata K, Kęsik K, Woźniak M. An Intelligent System for Monitoring Skin Diseases. *Sensors (Basel)*. 2018;18(8):2552. Published 2018 Aug 4. http://doi.org/10.3390/s18082552

Harangi B. Skin lesion classification with ensembles of deep convolutional neural networks. J Biomed Inform. 2018 Oct;86:25-32. http://doi.org/10.1016/j.jbi.2018.08.006. Epub 2018 Aug 10. PMID: 30103029.

Messadi M, Bessaid A, Taleb-Ahmed A. Extraction of specific parameters for skin tumour classification. *J Med Eng Technol*. 2009;33(4):288-295. http://doi.org/10.1080/03091900802451315

Stanley RJ, Stoecker WV, Moss RH. A relative color approach to color discrimination for malignant melanoma detection in dermoscopy images. *Skin Res Technol*. 2007;13(1):62-72. http://doi.org/10.1111/j.1600-0846.2007.00192.x

Gareau DS, Correa da Rosa J, Yagerman S, et al. Digital imaging biomarkers feed machine learning for melanoma screening. *Exp Dermatol*. 2017;26(7):615-618. http://doi.org/10.1111/exd.13250

Dascalu A, David EO. Skin cancer detection by deep learning and sound analysis algorithms: A prospective clinical study of an elementary dermoscope. *EBioMedicine*. 2019;43:107-113. http://doi.org/10.1016/j.ebiom.2019.04.055

Foahom Gouabou AC, Damoiseaux JL, Monnier J, Iguernaissi R, Moudafi A, Merad D. Ensemble Method of Convolutional Neural Networks with Directed Acyclic Graph Using Dermoscopic Images: Melanoma Detection Application. *Sensors (Basel)*. 2021;21(12):3999. Published 2021 Jun 10. http://doi.org/10.3390/s21123999

Phillips M, Greenhalgh J, Marsden H, Palamaras I. Detection of Malignant Melanoma Using Artificial Intelligence: An Observational Study of Diagnostic Accuracy. Dermatol Pract Concept. 2019 Dec 31;10(1):e2020011. doi: 10.5826/dpc.1001a11. PMID: 31921498; PMCID: PMC6936633.

Sondermann W, Utikal JS, Enk AH, Schadendorf D, Klode J, Hauschild A, Weichenthal M, French LE, Berking C, Schilling B, Haferkamp S, Fröhling S, von Kalle C, Brinker TJ. Prediction of melanoma evolution in melanocytic nevi via artificial intelligence: A call for prospective data. Eur J Cancer. 2019 Sep;119:30-34. http://doi.org/10.1016/j.ejca.2019.07.009. Epub 2019 Aug 8. Erratum in: Eur J Cancer. 2019 Dec;123:171. PMID: 31401471.

Efimenko M, Ignatev A, Koshechkin K. Review of medical image recognition technologies to detect melanomas using neural networks. *BMC Bioinformatics*. 2020;21(Suppl 11):270. Published 2020 Sep 14. http://doi.org/10.1186/s12859-020-03615-1

Nelson CA, Pérez-Chada LM, Creadore A, et al. Patient Perspectives on the Use of Artificial Intelligence for Skin Cancer Screening: A Qualitative Study. *JAMA Dermatol*. 2020;156(5):501-512. http://doi.org/10.1001/jamadermatol.2019.5014

El-Khatib H, Popescu D, Ichim L. Deep Learning-Based Methods for Automatic Diagnosis of Skin Lesions. *Sensors (Basel)*. 2020;20(6):1753. Published 2020 Mar 21. http://doi.org/10.3390/s20061753. PMID: 32245258; PMCID: PMC7147720.

Brinker TJ, Hekler A, Enk AH, Berking C, Haferkamp S, Hauschild A, Weichenthal M, Klode J, Schadendorf D, Holland-Letz T, von Kalle C, Fröhling S, Schilling B, Utikal JS. Deep neural networks are superior to dermatologists in melanoma image classification. Eur J Cancer. 2019 Sep;119:11-17. http://doi.org/10.1016/j.ejca.2019.05.023. Epub 2019 Aug 8. PMID: 31401469.