SPAST Open Access Research

Useful Datasets and Very Recent Approach for Melanoma Image Classification.

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Abstract

The growing incidence of skin cancers, coupled with low awareness among the population fuels interest in developing computer-assisted diagnostics solutions for skin cancer classification. A large number of data sets on skin lesions are publicly available and researchers have developed machine learning solutions to distinguish malignant from benign skin lesions aimed both to support the doctors and as mobile applications useful in self-diagnosis. The Computer Aided Diagnosis (CAD) systems are still in the very early stages of clinical application: in this review, we focus on the latest approaches used for image-based solutions for skin cancer diagnosis, highlighting the necessary future directions to improve these artificial intelligence systems.

Keywords: Deep Learning; Multiple Instance Learning; Melanoma Detection.

1. Introduction

The World Health Organization certifies that more than 57,000 people have died from melanoma and there are more than 320,000 new cases in 2020 (see Figure 1).

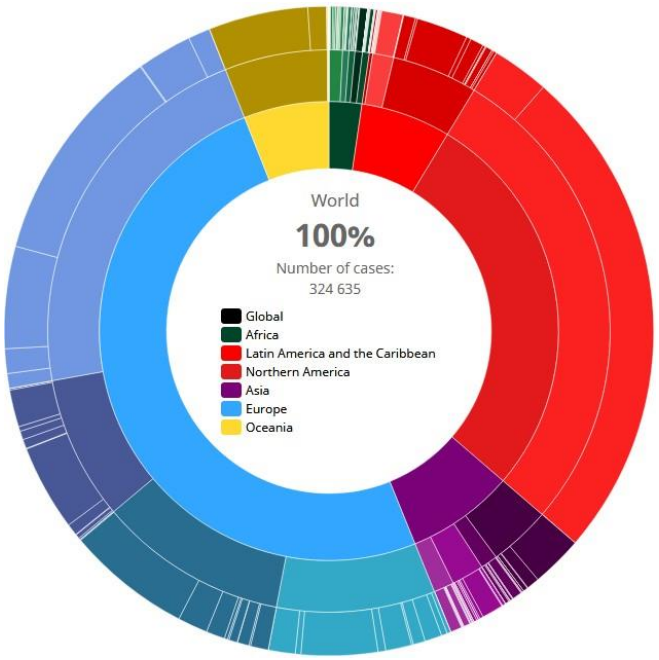

Figure 1. Number of melanoma in 2020, all age [1]

The reported data testify that melanoma affects the populations of all geographical areas of the world and in particular those of Europe (50.1 \% of total cases) and North America (27.7 \% of total cases). Melanoma ranks 5th for age-standardized (World) incidence and mortality rates in 2020, for both males and females, considering all ages [1].

Despite the worrying scenario in terms of both new cases and deaths, if melanoma is identified by early diagnosis it is a treatable type of cancer. However, once disease progresses beyond the skin, survival rate is poor: melanoma is the deadliest form of skin cancer [2].

Specific clinical protocols such as the ABCDE [3] rule and the 7-PCL [4] are adopted as a guideline for identifying lesions from an early stage. The ABCDE rule, which is the most commonly adopted, suggests monitoring symmetry, irregularity of the edges, colors of the lesion, its extension and evolution over time.

The importance of the early diagnosis of melanoma together with the needs of the follow-up of the lesions over time, has resulted in automatic solutions for the analysis of skin lesions.

In particular, Computer Aided Diagnosis (CAD) systems were born as dedicated frameworks to support skin analyzes. These systems include key steps: image acquisition, pre-processing, segmentation, feature extraction and selection, and finally lesion classification (see Figure. 2).

Each step poses significant challenges for the whole process to be effective. Among the most used techniques for image acquisition, dermatoscopy imaging, also known as epiluminescence microscopy (ELM), appears, which allows much more detailed images. In particular, advanced acquisition techniques such as dermatoscopy and confocal microscopy allow a detailed visualization of lesions and risk stratification [5, 6]. The adoption of advanced imaging techniques and high-resolution cameras have facilitated the

Received: 15-01-2021 Under review Pre-peer review

collection of high-quality data on skin cancer from patients around the world [7, 8]. The result is the availability of datasets of skin lesions with key expert annotations to create automated CAD solutions for diagnosing melanoma and other skin cancers. Artificial intelligence solutions for skin cancer diagnosis can rely on high-speed, affordable internet, computing power and storage security to manage and share skin cancer datasets.

Scalability across multiple devices, platforms and operating systems must not be overlooked, which makes the various solutions proposed by the scientific community modern and flexible medical tools. The purpose of this review is to provide the reader with a broad overview of the context of melanoma image classification, referring both to some recent Machine Learning approaches for Melanoma image classification.

2. Computer Aided Diagnosis Systems

There are many machine learning solutions proposed to allow the understanding of meaningful patterns from digital data. Techniques such as feature selection, transfer learning and multitasking learning are increasingly used in many medical imaging applications [9, 10]. The diffusion of medical datasets containing skin lesions images, together with the emerging role played by machine learning approaches, mean that the diagnosis of melanoma can be supported by using the latest generation of automated analysis tools such as computer-assisted diagnosis (CAD) systems which support non-invasive diagnoses by specialists. A specific CAD for automatic skin lesion analysis consists of the following basic steps: Image Acquisition, Image Pre-Processing, Segmentation, Feature Extraction and Selection, and finally Classification.

Figure 2. Fundamental Steps of CAD Systems

The task for which CAD systems are proposed is to provide a support to the diagnosis of the specialist, aimed at an easier identification of melanoma from the initial stage: this goal is pursued by carrying out an automatic analysis of the lesion images by adopting specific features.

Various medical protocols including the ABCDE [11] rule, the seven-point checklist [12], the three-point checklist [13] and the Menzies method [14], are a starting point for the development of diagnostic frameworks that allow increasingly reliable diagnoses and compromise the management of data from heterogeneous sources.

As mentioned, the epiluminescence technique (ELM) is enjoying considerable success in the field of dermatoscopic imaging techniques. A crucial aspect is linked to the optimization of the images to be analyzed, providing both the reduction of technical acquisition defects and of various artifacts, such as hair, which may be present in dermoscopic images [15, 16].

The segmentation is of fundamental importance before proceeding to the feature extraction phase; the image is divided into sub-regions according to criteria of homogeneity with regard to properties such as luminance, color and texture, or rather geometric. At the end of the segmentation phase the lesion comes localized the lesion, and it is possible to extract the characteristics of interest of interest that will allow to train the classifier to provide the result of the automatic investigation.

Despite the advances in imaging techniques and the continuous proposals for artificial intelligence algorithms, there are a number of drawbacks such as the extreme similarity of melanoma to other skin lesions such as dysplastic nevi.

Several approaches and algorithms have been proposed in the last decades, mostly with the main goal related to the dichotomous distinction of melanoma from benign lesions. Some challenges therefore remain under-addressed such as that of the classification of melanoma by dysplastic moles or in fact unaddressed such as the classification of dysplastic nevi against common ones, important in order to correctly evaluate the predisposition to the onset of melanoma in subjects affected by Dysplastic Nevi Syndrome (DNS) [17, 18, 19].

Currently the dermatological examination takes place through visual inspection of the enlargement of the lesion obtained with polarized light instruments. The diagnosis conducted by the specialist, however, also takes into account the patient's history, his ethnicity, and also the behavior related to exposure to the sun. When a suspicious skin lesion is found, a histological examination is typically recommended to provide a diagnosis, or if the presence of juvenile melanoma is suspected, a shorter follow-up of the lesion. Spitz nevus, also known as juvenile melanoma, is a nevus found mainly in young people (see Figure 3). It has a reddish color and is characterized by a rapid growth limited in time [20]. It appears to be made up of giant cells with little pigment, spindle and/or epithelioid with large nucleus and evident nucleoli, extended up to the reticular dermis. Observing a suspected pigmented lesion usually involves invasive surgical removal treatment as the first option.

On the other hand, however, when the conditions exist, both the young patients and their parents first evaluate a monitoring in a shorter time, in order to avoid scarring in exposed parts of the body. The follow-up procedures usually

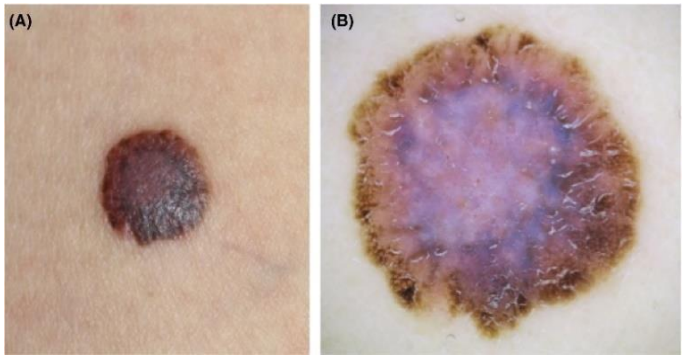

Figure 3. Spitz nevus: (a) at early and (b) at developed

include monitoring of Spitz's nevi every six months, while that of atypical nevi every three months. The possibility of being able to carry out detailed monitoring avoids uncertainties in the diagnosis and allows to better identify the surface of the lesion to be removed.

3. Publicly dermoscopic datasets for skin cancer

The purpose of the present work is to provide the reader with a broad overview of the context of melanoma image classification, referring both to the available data sets and to some recent approaches through which results of interest are being obtained. Recent work shows that the performance of machine learning-based frameworks is comparable with the dermatologists' diagnostic performance on melanoma detection.

More and more datasets are being made available to researchers. Below is a brief description of the free ones that contain images obtained through a dermatoscope.

A problem that must certainly be addressed in this context consists in the choice of the dataset to be used for the experimental phases. Often the datasets are created to support specific types of analysis as we will describe in detail below. Among the free public datasets that contain dermatoscopic images we mention:

1) **MED-NODE** Dataset [21]: It consists of 70 melanoma images and 100 nevus images from the digital image archive of the Department of Dermatology of the University Medical Center of Groningen (UMCG). This dataset is available free for download for research. This dataset contains only melanomas and superficial spreading nevi. The images of the pigmented skin lesions are from patients of Caucasian origin. For each image, the diagnosis available was verified by the medical correspondence of the Department of Dermatology. Rare clinical variants, previously treated and / or secondarily infected skin diseases are not included in the dataset. A region of interest which contains healthy skin and a lesion is manually selected from each image. Hair was manually removed using Dullrazor software [22]. The authors have made the anonymous and pre-processed images publicly available at http://www.cs.rug.nl/~imaging/databases/melanoma_naevi

2) **PH^2** Dataset [23]: The PH^2 dataset contains 200 dermoscopic images divided into 40 cases of melanoma 80 of atypical moles and 80 cases of common moles). You can download it for free after filling out an online registration form. Dermoscopic images come from the dermatology service of Pedro Hispano Hospital (Matosinhos, Portugal) and are obteined via the Tuebinger Mole Analyzer system using a 20x magnification. They are 8-bit RGB color images with a resolution of 768x560 pixels.

The PH^2 database includes medical annotation of all images, i.e. medical segmentation of the lesion, clinical and histological diagnosis and evaluation of different dermoscopic criteria.

The images can be found in a specific section of the site https://www.fc.up.pt/addi/ph2%20database.html. We used this dataset to verify the classification performance of MIL approaches, obtaining the other excellent results [24, 25, 26].

3) **Derm7pt** [27]: This dataset contains 1011 dermoscopic images (252 cases of melanoma and 759 nevi), with 7-point checklist criteria. In [27], the authors propose a multi-task deep convolutional neural network, trained on multimodal data (clinical and dermoscopic images and patient metadata), to classify 7-point melanoma checklist criteria and diagnose skin lesions. This dataset (images and metadata) is publicly available online at http://derm.cs.sfu.ca

4) **ISIC Archive**: the gallery of the ISIC archive collects arises from the juxtaposition of different datasets on clinical and dermoscopic skin lesions, including the ISIC Challenges [28], HAM10000 [29] and BCN20000 [30] datasets. Globally ISIC contains over 23,000 images of skin lesions, each labelled "benign" or "malignant". The archive can be found here: https://www.isic-archive.com/#!/onlyHeaderTop/gallery.

This dataset was created to allow the testing of applications based on neural networks for the automated diagnosis of skin lesions, overcoming the problem of the small size and lack of diversity of the available data sets of dermatoscopic images. Specifically, for this use, the HAM10000 data set ("Human versus Machine with 10,000 Training Images") was prepared, which contains dermatoscopic images from different populations from heterogeneous sources. This benchmark dataset can be used for machine learning and for comparisons with human experts. BCN20000 dataset, consists of 19,424 dermoscopic images of skin lesions captured in the facilities of the Hospital Clínic in Barcelona. BCN20000 arises from the need to support the classification studies of dermoscopic images of skin cancer, also including lesions in difficult positions (nails and mucosa) and large and hypopigmented lesions that cannot be captured by dermoscopy.

5) **Dermnet NZ** [31]: Dermnet NZ was born from the fusion of collections of dermoscopic and histological clinical images of various skin diseases, particularly suitable for academic research purposes. They have additional high-

resolution images for purchase. Home photo-monitoring of skin and moles should not replace a visit to the doctor. DermNet NZ provides authoritative information on skin diseases, conditions and follow-up useful for dermatologists, medical students and researchers. It currently contains more than 2,300 pages and a library of 25,000 dermatology images provided and reviewed by health professionals and students from New Zealand and other countries, including the United States, United Kingdom, Canada, Mexico, Indonesia and Sri Lanka.
On line medical courses for the continuing education of dermatologists are also provided on the website. An interactive tool, named DermDiag, allows users to sign ever more specific levels of information about their skin condition, starting from the location of the lesion.
The diagnoses provided are classified from Common to Rare and the user is provided with images of each potential diagnosis, along with the clinical characteristics of each condition.

Some research [32] has shown promising results obtained through machine learning algorithms for the assessment of melanoma risk applied to clinical images; however, there is still a long way to go before individual citizens can obtain an effective automatic risk diagnosis through a smartphone.
In fact, the British Association of Dermatologists announced that apps that aim to detect or diagnose lesions based on smartphone photos should be treated with caution [33].
Nevertheless, the proposal of mobile applications is always growing and is divided into solutions that integrate the use of the app in the context of tele-dermatology services that involve interaction with other patients and of course with experienced doctors [34].

4. Recent approaches for Melanoma image classification

In the classification step, the information extracted in the previous phases is used to produce diagnosis on the dermoscopic images. The dichotomous distinction between the two classes of melanoma and benign nevus and the determination of a probability value of an image to belong to a specific class of skin lesion, are possible results.
In recent years, deep learning appears to be among the most widely reported artificial intelligence approaches.
There remain a series of grey areas related to this approach, some of which animate research in different directions such as Transfer Learning and Multiple Instance Learning.
In the following two subsections we dwell on the recent results obtained with models based on deep learning and on multiple instance learning respectively, referring a brief discussion to the final paragraph.

4.1 Multiple Instance Learning recent contributions

This standard MIL problem is formulated according the standard MIL assumption: an image (referred as bag) is positive if it contains at least a positive sub-image (referred as instance) and it is negative if it does not contain any positive sub-image [35].
The MIL paradigm it is very suitable for image classification: in order to classify an image within a particular object, it's enough to look only at some sub-regions (instances) of the image (bag): with respect to a classical supervised approach MIL obtains global information from local detection.
The MIL paradigm is mostly promising in the field of medical image diagnostics where local analysis is relevant.
In [36], a multi-instance learning framework was inserted to face the task of recognizing skin biopsy images' features. Other approaches based on color features have not been able to directly recognize the characteristics of skin biopsy images due to the color changes present in the images. Through the multiple instance learning approach the authors used texture features to express each instance as a vector expression. Therefore, through the application of multi-instance learning algorithms, the proposed method showed to be effective and acceptable for medical analysis.
In [19], the authors highlight how the current debate on dysplastic nevi syndrome (DNS), impose new classification tasks among skin lesions. In fact, people with DNS, who typically have large numbers of moles throughout the body, are more prone to onset of melanoma. The use of a multiple instances learning algorithm, which uses spherical separation surfaces, is proposed to discriminate melanoma from dysplastic nevi and outline the complex challenge of classification of dysplastic nevi from common ones.
In [24], the authors present an application to melanoma detection of a multiple instance learning (MIL) approach, whose objective is to discriminate between positive and negative sets of items. Under the MIL assumption, the proposed approach fits very well with images classification, since an image (bag) is in general classified on the basis of some its sub-regions (instances).
Thought the application of a MIL algorithm on PH^2 dataset constituted by color dermoscopic images, the authors discriminate between melanomas (positive images) and common nevi (negative images). In comparison with standard classification approaches, such as the well-known Support Vector Machine, the proposed method performs very well in terms both of accuracy and sensitivity.
In particular, using leave-one-out validation, they have obtained good performance of classification (accuracy = 92.50\%, sensitivity = 97.50\% and specificity = 87.50\%), demonstrating that MIL techniques could be at the basis of more sophisticated tools useful for melanoma detection.
In [25], the authors presented a preliminary analysis of some MIL classification techniques, using color and texture features on a data set constituted by plain photographies, to which no pre-processing technique has been applied. Also in this case MIL techniques guarantee better classification performances respect to classical supervised approaches, opening new horizons regarding the creation of self-diagnosis systems for accessible skin lesions, emphasized by a huge innovation of cameras, smartphones technology and wearable devices. In light of recent developments MIL technique could be the basis of more sophisticated tools useful for detecting skin lesions.

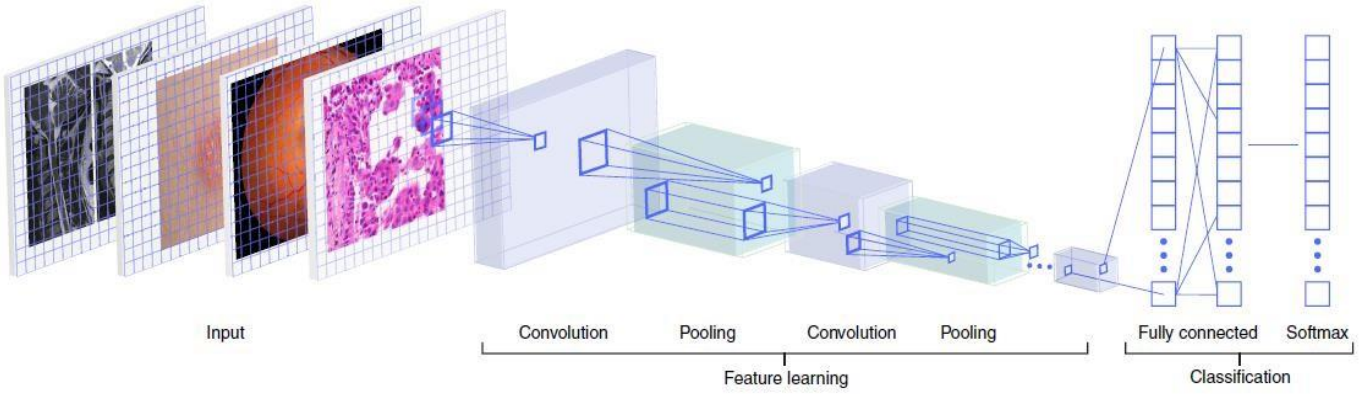

Figure 4: CNNs take input images and transform them using convolutional, pooling, and fully connected layers, into flattened vectors.

4.2 Deep Learning recent contributions

Scientific and technological advancement has made systems completely designed by humans obsolete, making them prefer systems trained by computers over sample data. The new evolutionary step consists in the use of features vector no longer handcrafted but learned directly from the model. Nowadays, automated extraction of relevant features from input data is at the heart of many deep learning algorithms. Convolutional Neural Networks (CNNs) are currently the most successful architecture for image analysis, ever since Krizhevsky et al. participated and won, the ImageNet challenge with AlexNet [37].

An example of a structure is shown in Figure 4 where the elements of the output vector (softmax layer) quantify the probability of the presence of the disease. To improve the accuracy of the performance, the internal parameters of the network layers are adapted iteratively during the training process.

CNNs are a class of deep feed-forward artificial neural networks, applied to data that can be represented in a grid structure such as 2d images. Taking inspiration from biological processes [38, 39], CNNs mimic the cerebral cortex that receives electro-chemicals impulses generated by the cornea. CNNs are shift-invariant or space invariant, thus inherently more efficient thanks to their shared-weights architectural feature and to be translational invariant [40, 41]. The key properties underlying the success of CNNs concern the *translational invariance* or the ability to recognize the same pattern in different shapes, positions and orientations within the image, the *multi-scale* or the ability to learn complex abstract structures in a hierarchical way and the *locality* which means that the activation of a neural path is based on the detection of a familiar pattern.

Among the strategy pursued to obtain results of interest, with transfer-learning a model pre-trained on similar activities is loaded and used for the new model to be carried out. In [42], the author presented a universal skin disease classification method by selecting models that have proven to perform well in the ILSVRC-2014 competition (i.e., VGG16, VGG19 and GoogleNet), then trained on the ImageNet dataset. These pre-trained models are then applied on the DermNet dataset, which contained more than 23,000 images of skin diseases. In the experimental evaluation, performed on the DermNet and OLE datasets, the proposed method obtained an accuracy of 73.1 \% Top-1 and 91.0 \% Top-5 on the Dermnet dataset and 69.5 \% accuracy Top-5 on the OLE dataset.

Similarly, in [43], the authors use a pre-trained model to detect skin lesions, achieving reduced training time with 85.8% accuracy in the 5-class test bench.

A powerful tool in the case of lack of data, or unbalanced datasets, is data augmentation: increase in data can in fact mitigate the effects of unbalanced data sets, with different class size of skin lesions or coming from heterogeneous data sources. Better results are obtained by adding augmented samples with different image transformations, such as rotation, random clipping, horizontal flipping and vertical, translation, cutting, color jitter and color space. The model's classification performance is better as demonstrated in [44]. The potential of deep learning has actually ignited the competition for the diagnostic capabilities of automatic solutions against those of specialists.

In [45], the authors propose a system able to segment skin lesions, as well as to analyze the detected area with surrounding tissue for melanoma detection. The ensamble of deep learning algorithms was tested on the ISIC-2016 dataset; the performances obtained with this framework were compared with 8 dermatologists for the classification of 100 skin lesions as benign or malignant. The proposed method has shown an accuracy of 76% and a specificity of 62% against 70.5% and 59% achieved by dermatologists.

Also in Haenssle et al. [46], the performance of the proposed learning method was compared with that of 58 dermatologists. The test set involves 100 cases (25 cases of melanoma and 75 benign lesions): the deep learning method achieved a sensitivity of 95% and a specificity of63.8%, while dermatologists had an average sensitivity of 86.6% and a specificity of 71.3%. The goodness of the predictive capacity of solutions based on deep learning algorithms has also been demonstrated on more numerous

datasets. In [47], the performance of 157 board-certified dermatologists at 12 German university hospitals was compared with a deep learning method (ResNet50). A convolutional neural network (CNN) received enhanced training with over then 12,000 open-source dermoscopic images. CNN outperformed 136 of 157 participating dermatologists in all hierarchical subgroups of dermoscopic melanoma image classification. In fact, the proposed method achieved a specificity of 69.2% and a sensitivity of 84.2%, while dermatologists achieved an overall sensitivity of 74.1%, and specificity of 60.0% on the dermoscopic dataset. Currently the solutions that adopt deep learning have a lot of application potential. In the context of dermatoscopy, however, there are still many challenges to be faced and overcome before arriving at a robust medical validation that allows real application both in terms of support tools for specialists and for the implementation of mobile apps recognized by health care organizations.

5. Challenges and Opportunities

The spread of melanoma, both in terms of diagnosed cases and deaths, as well as for the growing availability of databases of dermoscopic images has increased the interest on tools for automatic classification of skin lesions. To date, there are a series of reservations about the applicability of machine learning models on dermoscopy even on deep learning. The imbalance between the classes of training datasets should not be underestimated. The risk consists in undermining the classification performance of the models, which can manifest over-fitting, thus losing in generalization. Once optimized also the issues related to image acquisition and pre-processing steps, it is possible to obtain different classification results depending on a series of factors such as the choice of features vectors which feed the classifiers [47-49].

Melanoma detection, and more generally, medical image processing, can benefit from recent advances in deep-learning-based methods. The growing interest in DL architectures also lies in the fact that the choice of features can be made through the model, but this aspect also constitutes one of the biggest reservations about DL solutions which involves the loss of sensitivity. The DL has an intrinsic "bias" that leads it to consider what appears to be very frequent in data to be true.

Despite the various claims of deep learning algorithms surpassing clinicians' performance in the diagnosis of skin cancer, there are far more challenges faced by these algorithms to become a complete diagnostic system. Typically, the experiments are performed in controlled settings, while the real-world diagnosis process requires taking into account a patient's ethnicity, skin, hair and eye color, occupation, illness, medicines, existing sun damage, the number of nevi, lifestyle habits and clinical history, the respond to previous treatments, and other information from the patient's medical records [50]. However, current deep learning models mainly rely on only patients' imaging data.

The performance of dermatologists, regardless of their experience, improves by knowing the patient's general clinical information: in [51], it is demonstrated that these are better than those offered by solutions based on deep learning algorithms. Clinical metadata to date are absent in the data sets on skin lesions also opening to clustering, or outlier detection issues [52, 53].

As mentioned, the solutions based on DL, if applied to skin lesions different from those on which they have been trained, risk leading to a diagnosis, sinning in possible different contextualizations of analysis. The complexity of recognizing recurrent patterns for skin cancers implies that deep learning algorithms work according to logics different from medical protocols such as the ABCDE rule.

As a result, although researchers try to demystify how deep learning algorithms work, the medical community looks to deep learning solutions as a black box, the reasons for which the diagnosis is not understood. In machine learning solutions without a deep approach, the model is instead instructed with handcrafted features that are similar to those of the medical protocols [54, 55]. This aspect marks a winning point in favour of frameworks that exploit the MIL approach.

Deep learning algorithms are very sensitive to the camera devices used to acquire the data and their performance degrades if a different type of camera device is used for testing. This places limitations for mobile applications whit images acquired from different cameras smartphones in different lighting conditions and distances. Indeed, patient-supplied skin images are affected by poor exposures and are often of low quality [56,57].

The delicate challenges that stand in the way of real-world applicability of automated dermoscopy solutions mean that computer vision companies and dermatologists must work together to improve the diagnostic accuracy of the used methods. Machine Learning has the potential to deliver a paradigm shift allows cost-effective, remotely accessible, and accurate healthcare solutions [58].

Automated tools which support melanoma detection since its early-stage, tracking its evolution in time, and which could even be remotely used, represents an unprecedented opportunity to improve the way to fight this aggressive form of skin cancer. The interaction of specialist with frameworks for diagnostic support, together with a cultural model oriented to greater population proactivity through mobile self-diagnostic tools, is an emerging recipe for achieving a significant reduction in melanoma's mortality rate.

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