ABSTRACT

The past years have seen a considerable increase in cancer cases. However, a cancer diagnosis is often complex and depends on the types of images provided for analysis. It requires highly skilled practitioners but is often time-consuming and error-prone. If Machine Learning and deep learning algorithms have been widely used, a comprehensive review of the techniques used from the pre-processing steps to the final prediction is lacking. With this review, we aim to provide a comprehensive overview of the current steps required in building efficient and accurate machine learning algorithm for cancer prediction, detection and classification. To do so, we compile the results of cancer related study using AI over the past years. We include various cancers that encompass different types of images, and therefore different related techniques. We show that tremendous improvements have been made in the early detection of cancerous tumors and tissues. The techniques used are various and often problem-tailored and our findings is confirmed through the study of a large number of research. Moreover, we investigate the approaches best suited for different types of images such as histology, dermoscopic, MRI, etc. With this work, we summarize the main finding over the past years in cancer detection using deep learning techniques. We discuss the challenges of cancer research related to the large discrepancies in the images, and we provide some notable results in the field for lung, breast, and skin cancers.

Keywords Machine learning, deep learning, cancer detection, cancer diagnosis, image analysis, computer vision

1 Introduction

In the past decade, the number of computer-aided-diagnosis (CAD) studies via Machine Learning (ML) and deep learning (DL) algorithms has grown exponentially and has seen an incredible spike in their applications, especially in the biomedical field [1,2,3,4,5]. Their use in cancer detection is numerous and allows for rapid diagnosis of different cancer types. The world has seen an impressive increase in cancer cases. Not only the number has continuously grown; but with around 9 million cancer deaths in 2017 worldwide, and 2 million new cases and 600 thousand cancer deaths in 2021 in the United States alone [7], the need for appropriate tools of detection and diagnosis is becoming more and more pressing both for accuracy and rapidity [8].

According to the American Cancer Society, the chances of survival over 5 years for an individual increase by 90% when cancers are detected early. Similarly, screening for breast cancers has resulted in a lower death risk of 20-40% [9,10]. However, lung cancers are detected in their later stages in 70% of the cases [11]. In addition to decreasing chances of survival, late cancer detection leads to potential outbreaks of cancerous cells in other parts of the body leading to metastasis which needs to be prevented at all costs and provide a challenge for machine learning techniques.

Amongst all cancers, the tracheal, bronchus, and lung cancers are the most prevalent ones with a little under 2 million deaths, closely followed by colon, stomach, and liver cancers (digestive tract cancers) with around 800 thousand deaths for the year of 2017. Over the past decades, the number of deaths has decreased in the age group of 50-69 but increased.
in the age group of 70+ year old, which shows improvement in health care received for cancer treatments allowing patients to recover and live longer [7].

While treatments are becoming more effective for some cancer types, early detection is still the most successful approach to improve the chances of recovery. Therefore, using machine learning and deep learning algorithms for diagnosis has gained traction in recent years. These algorithms allow for the rapid assessment of tumorous tissues with decreased human bias. They also lead to the earlier detection of cancers, i.e., at stages for which tumors are sometimes difficult to analyze by the human eye. Before discussing the different algorithms that have been developed to improve diagnosis, we briefly introduce the types of image that are often used in cancer detection as well as the three cancers chosen to conduct this work.

### 1.1 Traditional cancer detection methods and image types

Cancer detection strongly depends on its type [14, 15, 16, 17]. For instance, skin cancers can be diagnosed provisionally using dermoscopic images and non-invasive techniques. The use of non-invasive techniques is not always possible, and is often complex; therefore, diagnosis requires complementary methods such as biopsies. Using different techniques means that images with different specificities will need to be analyzed. In turn, it impacts the type of machine learning technique and the training process used to obtain a diagnosis. Hereafter, we give a quick overview of the different types of images primarily used in cancer detection and their related characteristics:

1. **Dermoscopic images**: These images are relevant to skin cancer detection. Dermoscopic images are direct images of a person’s skin taken by a dermatologist for diagnosis purposes. The advantage of such an approach is that it is non-invasive. Nonetheless, images often have different characteristics due to various technical aspects such as camera angle, lighting, or contrast. These differences make images complicated to analyze. In turn, images alone are often insufficient to lead to a correct diagnosis. However, such images are ideally suited to train Artificial Intelligence (AI) models. Performing a biopsy is required to confirm the diagnosis which, in turn, provides labeled databases.

2. **X-Ray and CT scans**: Computerized Tomographic (CT) scans are often used in the early detection of lung and brain cancers (also found in some other cases) [20, 21, 22]. They consist of a collection of X-ray images, taken from multiple angles, and have the advantage of providing a 3D rendering of tumors. CT scans allow for the rapid detection of abnormal growth. However, they can be expensive and complex to analyze. These grayscale images are often available from medical databases since CT scans are typical analyses for most cancer types. Since CT scans include many images, they readily lead to large training datasets which are necessary to train accurate models [20]. Moreover, these images have standardized characteristics, thus decreasing the number of pre-processing steps needed.

3. **Histology**: Histology images are obtained from biopsies and provide direct insight into the cellular system of the patient. They allow for cancer detection at an early stage of the disease, before any physical manifestations (i.e., melanoma in skin cancers), and are often used during breast cancer detection. The detection of cancerous tumors or tissues takes place on images with Hematoxylin and Eosin (H&E) stains. The dye colors each image and allows to visualize cell nuclei and membranes. However, the intensity of the color depends on the amount of dye employed and is not standardized. These images are also very large, which complicates the analysis of large datasets. Histology images are of great significance as they allow for the determination of cancer stage and cancer treatment [24].

Deep learning techniques can also be applied to other types of images. These include Raman spectroscopy, mammography, ultrasound images, etc. [15, 25, 26, 27]. For instance, ultrasound images can be used for breast and thyroid cancer detection, and deep learning approaches have been developed for these applications. In this review, we focus on three specific types of cancer: lung, skin, and breast cancers since these cancers have been the most extensively studied in the biomedical field and provide a comprehensive access to the various techniques and image types.

### 1.2 Types of cancers studied in the review

As discussed by Hanahan and Weinberg in their pioneering work [29], the formation of tumors is a multistep process that results from genetic alterations. These genetic alterations lead to the gradual transformation of normal cells into malignant cells. The latter have several acquired capabilities, including their ability to be insensitive to antigrowth signals, mimic growth signals, evade apoptosis, self-replicate in a limitless manner, sustain angiogenesis and invade tissues and lead to metastasis. While some cancers, like leukemia, do not cause tumors to form, tumors are found commonly in many types of cancers, such as lung, skin, and breast cancers. In many cases, the presence of a tumor is the most visible symptom that initiates the diagnosis process [15]. We focus here on tumorous cancers that provide
adequate imaging access with different technical challenges. Moreover, since all nodules are not necessarily cancerous it increases the importance of diagnosis and appropriate tools to differentiate between the ones that are and the ones that are not cancerous. As discussed in section 1.1, each type of cancer leads to different categories of images and, as a result, involves specific machine learning and deep learning approaches. In the case of lung cancer, many abnormalities may appear in the chest cavity and are often left untreated which, in turn, makes the diagnosis process complex [30]. For breast cancer, the challenge is to analyze both the tumor-like masses and also the onset of other processes, such as calcification, which are often early signs of the disease [31]. Thus, we examine here studies performed primarily on breast, lung, and skin cancers. Moreover, figure 1 shows an analysis of the studies published between 2017 and 2022. This plot shows that breast, lung, and skin cancers are the most studied and lend themselves to deep learning approaches.

The current literature is lacking a comprehensive overview of machine learning and deep techniques used to detect, classify or predict cancer tumors and tissues. Thus, in this review, we aim to offer a detailed analysis of the techniques used on various image and tumor types. This work aims to encompass various types of images and not limit itself to one specific image type. The contributions of this review are multiple and include: (i) a systematic approach to a large number of papers published in the recent years relating research in cancer detection using machine learning or deep learning, (ii) an overview of the pre-processing techniques commonly used for different image types, (iii) an analysis of the performance of the most common deep learning models and their classifier, and (iv) a comprehensive comparison of pre-trained models most often used in cancer diagnosis research. To do so, we start by presenting the review method used to select papers, including keywords, and inclusion and exclusion criteria. Then, we discuss the pre-processing and data augmentation techniques used to develop machine learning and deep learning models. Finally, we discuss the different feature extraction methods employed, from histogram analysis to convolutional layers, and detail the different classifiers so obtained and their applications.

2 Review method

2.1 Paper selection

Papers for this study were selected using both the PubMed and BVS databases. A combination of the following keywords was used: “Machine learning, deep learning”, “image classification”, “cancer detection” and “lung, breast and skin cancer” for both databases. After omitting books, we obtained a total of 582 scientific papers for the period between 2019 and 2021.
2.2 Criteria for exclusion and inclusion

We first removed all duplicates leading to a total of 363 remaining papers. We also discarded all articles for which full papers are not accessible, papers written in a different language from English, and book chapters. Then, some papers were removed on the basis of titles, which fell outside the scope of this review, leading to 234 papers.

3 Discussion

Surveys and reviews have been published on a given type of cancer and the corresponding imaging technique. These include lung nodules from CT scans,[4, 32, 33, 34, 35, 36, 37] dermoscopic images for skin cancers,[38, 39, 40] and the application of AI for breast cancers diagnosis[41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51]. Moreover, reviews have often focused on specific aspects, such as, e.g., the comparison of transfer learning approaches [52], and a comprehensive review of the field is missing.[6, 53, 54]

Previously published reviews have agreed on the increased use of deep learning in cancer detection methods.[33, 42] Therefore, we focus here on the applications of deep learning approaches in segmentation, detection, or classification/prediction tasks. We add that, in some cases, a combination of 2 (or more) deep learning methods is employed to improve performance.[55] In the next section, we discuss all three aspects as they each have significant consequences on performance.

The discussion follows the general workflow of deep learning algorithms shown in figure 2. We first discuss the input type, and the pre-processing steps. We then move on to the feature extraction aspect of deep learning, before discussing the impact of classifiers on models’ performance. We conclude with the analysis of some pre-trained models and additional general results.

3.1 Pre-processing and image handling

It is now widely recognized that the pre-processing of images has a significant impact on the results for all machine learning and deep learning approaches.[56] However, the choice of a specific pre-processing technique depends on the image type, but also on the database.[57, 58] Therefore, the choice of the database is a significant step in the building of a machine learning/deep learning algorithm. An important analysis is done on the preparation of the database itself, which often comes in a non-practical format for machine learning usage. From handling labeling to pre-classification, this step allows for a properly built initial database. In addition, the database is often time separated into different categories to perform training, validation and testing of the model. A most common ratio being 80% of the images to train the model and 20% to test its performance.

Medical images are significantly different than regular images and, as such, require specific processing.[59] Indeed, low contrast images can lead to a difficult visualization of features.[60] Pre-processing can include many different approaches: from handling large images,[61, 62, 63, 64] to using segmentation.[65, 66, 67, 68] In some cases, the images themselves need to be modified to be fully usable. An example of pre-processing operation is the removal of pectoral muscles in breast cancer studies.[69] Additional applications include contrast enhancement, color change, boundary extraction,[70, 71] and noise reduction.[71] For instance, Boundary extraction of skin cancer was used by Saba et al. to increase the performance of their deep learning model on dermoscopic images.[70] Similarly, the use of noise reduction by Wei et al. improves the quality of the image fed to the network, thus enhancing the model’s ability to differentiate between different cancer types.[71] Additionally, Làng et al. successfully used spatial and temporal subtraction to obtain a better contrast in breast cancer analysis.[72]

As discussed in section 1.1, histology images are often used for cancer diagnosis. The challenge here is to work with images of a gigabyte size, similar to those used for skin cancer analysis.[61] A method that showed successful results when combined with CNN models is the patching technique.[62, 73, 74, 75] By reducing the image size, the work becomes less computationally intensive.[63] Indeed, patching of Whole Slide Imaging (WSI) can avoid deep segmentation, while still providing high accuracy, specificity, and sensitivity (96.91%, 96.18%, and 97.24% respectively for the study of breast cancers.[64]) Similar results were obtained on lung cancers.[76] Additionally, the large size of histological images can be decreased with segmentation steps.[77] However, new models have been developed recently to provide morphological features from WSI without patching.[78] since even highly accurate models on patch-level can fail to identify the tumor bed correctly.[74] This technique has the advantage of removing some of the pre-processing steps, including finding the Region Of Interest (ROI).[79, 80, 81, 82] In addition, it also seems to yield better results when combined with large structure models.[74]

In addition to the treatment of large images, medical databases often come with limitations, e.g., a high imbalance between classes, or a lack of annotations. The pre-processing step often allows for the improvement of models’
Figure 2: Workflow for deep learning and machine learning approaches to cancer detection.
performances. For instance, skin cancer datasets are often imbalanced. To address this issue, mask-RCNN methods have been employed and have led to improvements in accuracy and other metrics [84]. Other studies on the example of breast cancer also report that pre-trained models can also solve this problem [84].

Data augmentation is now widely used, as reflected by the literature. It allows for the extension of the original database. The application of the horizontal and vertical flipping of images improves the overall accuracy of a model [68]. Similarly, data augmentation reduces the skewness of skin cancer datasets and their imbalance [68]. Variations in dataset size and balance can strongly impact the accuracy of the model [83], and the benefits of using data augmentation have been highlighted in recent work [77]. The lack of data in the medical field often results in incorrect diagnoses with a large number of false positives [86, 87, 88]. To address this issue, novel data augmentation techniques, such as combinations of a graph convolutional network (GCN) and a convolution neural network (CNN), have been developed and have led to a significant improvement in the accuracy of the models [89, 90]. Traditional Generative Adversarial Networks (GAN) algorithms can also be used to tailor data augmentation in skin cancer detection [24, 91]. Similarly, additional data can be generated with a GAN-based radiomics model and TED-GAN algorithms [92, 93]. The latter provides additional skin cancer images and improves the accuracy of the classifier from 66% to 92.5% [94]. Moreover, data augmentation with ROI identification leads to significant improvements in the performance of CNNs, as shown by increases in accuracy and precision [95]. Similar conclusions hold for pre-trained models as well [96]. Another data augmentation technique, known as random cropping center (RCC), also enhances the performance of deep learning models [97].

In addition, the scarcity of datasets with annotated images has slowed down progress. As a result, recent studies are focusing on segmentation and automatic annotation of X-ray images, which would be otherwise extremely time-consuming [98]. Alternative annotation techniques are currently under work to circumvent the problem. For instance, Lotter et al.’s method leverages localization-based information and out-performs [99]. Pre-processing also consists of retrieving annotations from the dataset, a time-consuming and costly task. To this end, the automatic labeling of histological images, powered by the use of confidence-boosting queries, has been developed [100].

Along with offering labeling solutions, segmentation provides many possibilities for feature extraction [67, 76], and is a crucial step in cancer detection [101, 102, 103, 104]. For instance, in breast cancer detection, one of the pre-processing steps consists of the identification, and sometimes removal, of pectoral muscles. Deep learning models have been used to this end in recent work [105]. Systematic comparisons between ML approaches, with or without segmentation, have been performed. They show that the impact of segmentation correlates with the type of model used for classification [106]. Higher success rates for diagnosis are obtained when segmentation and diagnosis tasks are two separate steps in the model [107, 108, 109, 110, 111], or when a succession of models, each dedicated to segmentation, detection, and classification process are employed [77]. Separating segmentation and classification tasks into a combination of a GAN model for segmentation and a CNN for classification led to a 99.28% specificity and a 98.75% accuracy [60]. It allows for the identification of relevant areas for diagnosis and can involve different techniques, from masks to combinations with histograms [111, 112]. Results are often improved through contrast enhancement [65, 66, 67, 113]. ROI extraction [114, 69, 115] increases the accuracy of CNN models as shown for skin cancer databases [116]. Image quality can also be improved by reducing the background noise [117]. In the case of WSI, the teams using the Otsu method for noise removal generally obtained better performance with accuracies up to 95% [37]. Similar results were obtained in studies on lung cancer studies [118]. Optical-based methods also lead to accuracy above 97% for breast cancer detection [119]. CNN models have also been used for segmentation purposes [120].

We add that the U-net model has been used on various types of medical images [107, 121, 122, 123, 124, 125, 126, 127]. Results show that its performance depends on the size of the nodules for lung cancer [107] and report 80% accuracy on dermoscopic images for skin cancer diagnosis [125]. For mammograms, segmentation is instrumental in locating the tumor [126, 127]. Similarly, mask R-CNN is widely used to locate a nodule in lung cancers [108], which is especially crucial when working on chest X-rays [73].

3.2 Feature extraction

Feature extraction generally takes place after the pre-processing step. It is a crucial step in the development of high-performance models, which often rely on a large number of features. For instance, a dataset with 782 features was recently used in breast cancer classification [24]. Assessing which features are the most relevant can be complex and has led to the design of feature-oriented techniques [128, 129, 130]. In this section, we focus on two types of feature extraction. First, we examine the case of low-level features and then turn to deep feature extraction.

The type of low-level features extracted relies on a human choice. For instance, histogram extraction, via e.g., HOG (histogram of gradients), is a common feature extracted for classification [131]. Examples of manually extracted features are fuzzy color histograms, RGB histograms, gray histograms, JPEG coefficient histograms, Haralick features, local binary partition histograms, and graph-based features. Low-level features can also include information on the
shape, texture, border irregularities, and color of skin cancers. To increase performance, algorithms such as SURF, Gabor filter (GFs), SIFT, ORB, and GLCM can also be used. Studies report an improvement in accuracy when radiomic features (shape of tumor/lesion, existence or lack of spicula, and texture of the sample) are used. Manually extracted features from local binary patterns and fed to an artificial neural network (ANN) can lead to a higher accuracy than some CNNs after deep-level feature extraction. However, manually extracted features are often not sufficient, particularly in skin cancer detection due to the similarity between lesions from one cancer to another.

Deep learning models are often used to optimize the feature design tasks. Machine learning algorithms can provide low-accuracy predictions in skin cancer classification as many parameters need to be accounted for (light and angle, among others). A CNN is often used in deep-level feature extraction. It is generally a great alternative to the manual extraction of features, as shown by 3D convolutional neural networks for lung CT scan. They have been used to transform 2D color patches into classifiable 1D descriptive vectors. Another advantage of feature extraction via deep learning is that it does not require any a priori knowledge and thus removes any potential bias. Many other applications of CNN models as features extractor have been reported. This includes bio-inspired CNN models for breast cancer classification was bio-inspired which detect abnormalities in histological images. Similarly, the BCHisto-Net model was developed to improve feature extraction on whole slide images in the case of breast cancer. However, deep-level features are generally associated with specific images and may not transfer to multiple classes easily. Overall, feature extraction with CNNs is very efficient with results of 97% accuracy reported for metastatic breast cancers. A CNN also allows for the extraction of several features simultaneously. Khan et al. show that CNNs can lead to the identification of the three main characteristics of breast cancers (lump, masses, and calcifications) and report an 88% accuracy for the classification between four types of cancers. Other studies have emphasized the significance of specific features, and the impact of the structure of the convolution-based model. Shu et al. show how the use of different types of pooling changes the accuracy of a CNN model for breast cancer detection. In addition, the use of a CNN for the extraction of relevant patches in mammography analysis, followed by the application of multiple-instance learning techniques, has led to an Area Under Curve (AUC) of 0.91. Transfer learning is also highly efficient for feature extraction and has led to very accurate results.

In addition to low-level and deep feature extractions, prior work has developed approaches for the extraction of mid-level features. While deep features (deep learning) and low-level handcrafted features (human learning) differ, one may obtain models of similar accuracy from these two types of features and learning. Therefore, combining extraction methods at the two levels can provide better detection models. For instance, recent work has shown that a combination of CNNs and handcrafted feature extraction techniques improves significantly the overall accuracy and addresses issues caused by small and imbalanced datasets. For breast cancer detection, such a combination leads to a 2% increase in accuracy with respect to the sole application of deep feature extraction. Similarly, multiple extraction features that leverage deep learning can be combined. For instance, a bi-linear convolutional neural network of VGG16 and VGG19 was proposed for the classification of lung cancers and breast cancers with a 94.2% accuracy. Fusions of CNNs with other pre-trained models, such as the ResNet50, for feature extraction, increased the AUC by 0.02 up to 0.94 for skin cancer detection. Feature extraction fusion has demonstrated a large improvement in models’ performance for several types of cancer. Dual pathways models have also been developed to study the impact of multiple features on the accuracy, and have led to improved results when compared to single pathway techniques. The combination of multiple feature types and the inclusion of parenchymal imaging features have also been found to result in increased accuracy.

Feature extraction may also consist of region extraction, for example, in the case of skin cancer. The combination of patient metadata with a CNN model-based feature extraction greatly improves the accuracy of models for skin cancer detection (from 73.69% to 92.34% accuracy). This requires having information on the patient (e.g., age, gender, anatomical position, among others), and, in turn, predictions do not rely solely on the images fed to the model. Novel structures have recently been proposed. An example is a BCHisto-Net model for the analysis of breast images, which extracts both local and global features and out-performs state-of-the-art classifiers.

3.3 Classifiers

After feature extraction, various algorithms can be applied to perform classification tasks. This includes Support Vector Machine (SVM) and Neural Networks (NN) models, among others. The SVM classifier is typically used in the study of optical images for breast or lung cancers. In recent years, machine learning methods were improved to compete with deep learning techniques. The so-called extreme learning machine method, with SVM and Naive Bayes (NB) classifiers, was devised to detect early calcification in breast cancer detection. This technique provided over 99% accuracy. SVM classifiers on handcrafted features led to 96% in breast cancers, and a combination of CNN for deep feature extraction with an SVM for classification was applied to build a skin cancer prediction model.
CART algorithm was developed for the analysis of Merkel cell carcinoma in skin cancer [156]. The SVM classifier showed very good results in breast cancer detection on handcrafted radiomic features [134], on MRI images [157], but also on microwave images [158]. A comparison of SVM, KNN, decision tree, and random forest (RF) classifiers for lung nodule classification shows that the decision tree is the least accurate, while SVM and KNN lead to an accuracy greater than 94% [131]. Similar results were obtained on other cancer types [63]. A study by Aswathy et al. used SVM for the classification of histology images of breast cancers. The results showed that SVM provided better accuracy (over 90%) than NN and RF [159]. A similar performance was also observed for lung nodule detection, with a 97.45% sensitivity rate [113]. This method is able to provide a low number of false positives. Furthermore, an SVM classifier for the multi-classification of skin cancers yields an accuracy of 98.99%, 97.54%, and 99.65% for data taken from different databases [132]. Finally, non-deep learning techniques, such as RF, have led to an accuracy of 83.51% in studies on lung nodules [160]. Other classifiers include attention classifiers [161, 61], in which attention networks are used to detect the position of lungs [161], and adversarial training for skin cancer detection [162] and lung cancers [163].

The efficiency of classifiers generally depends on the type of cancer detection tasks and on the type of features extracted. For instance, in some cases, SVM classifiers can lead to a higher accuracy than softmax classifiers on lung nodules classification [148]. Similarly, features extracted with direct convolutional neural networks and fed to a SVM classifier have been reported to be highly efficient for breast cancer classification [150, 64]. Ensemble learning can also improve the performance of a classifier. Ensemble learning consists of assembling various machine learning classifiers and averaging their predictions [83, 164].

Tailoring the characteristics of the classifier is often necessary to improve accuracy. Radiomic machine learning classifiers, implemented with an Elastic Net regularization for logistic regression, can double the rate of early detection of lung cancer patients with an AUC of 0.89 [21]. Similarly, classifiers can be optimized, e.g., with the Whale optimization algorithm, and lead to an accuracy of 95% for skin cancer classification [165]. Loss function options are often explored to assess performance. For instance, Wang et al. provide an alternate loss function to that commonly used in softmax classifiers with a double-classifier [166]. Moreover, focal loss functions can improve accuracy (up to 97.2%) for lung cancer classification, while retaining a similar sensitivity and specificity [167]. The penalty loss function also showed great promise in reducing the number of false positives for lung cancer classification, leading to an accuracy of 91.60% [168]. These results emphasize the need for the appropriate tuning of a model. Johny et al. demonstrate the importance of fine-tuning CNN models, with dynamical learning rates resulting in better performance with a maximum accuracy of 91.84% [82].

### 3.4 Transfer learning and pre-trained models

Several studies leverage transfer learning via the use of pre-trained models. In general, pre-trained models are trained initially on the extensive ImageNet database [169]. Pre-trained models are then applied to cancer detection and classification [70, 62, 64, 141, 170, 151, 171, 62]. However, the ImageNet database does not focus on biomedical images. It, in turn, requires that the models be partially re-trained to be efficient for cancer detection. Several pre-trained models were recently developed for biomedical applications [172, 97, 173]. These biomedically-oriented pre-trained models share a similar structure with popular pre-trained models, such as VGG16 [174], and have been reported to yield an accuracy up to 98%. To address the issue of generalization for models pre-trained on medical images, Gu et al. have proposed a two-step training. The model is first pre-trained on the ImageNet database and then fine-tuned on two different databases of dermoscopic images [175]. Moreover, Gu et al. showed that adversarial domain adaptation allows for better generalization. This approach also addresses issues arising from small and imbalanced databases by carrying out part of the training on a larger dataset. For instance, using Mask-DenseNet+ on an imbalanced dataset led to 90% accuracy and 0.95 AUC [83].

Pre-trained models play a major role in all steps, from detection [176] to segmentation. For instance, AlexNet and ResNet50 can be used for skin cancer detection [136], while ResNet50 can be used for the segmentation of lung nodules, leading to an accuracy of 87.3% [107]. A study recently showed that region-based CNN (R-CNN) and RetinaNet modes provided the best performance for lung nodules detection [176]. The accuracy was also shown to increase when combined with the patching method for breast cancer analysis [63].

Even for a given cancer type, the performance of pre-trained models correlates with the image type. While models like EfficientNet-B3 are well suited to WSI-related diagnosis [74, 177], others perform better on dermoscopic images. Similarly, studies indicate that VGG16 performs well for the binary classification of dermoscopic images [178], while ResNet50, Inception, and DenseNet provide better accuracy for multi-class prediction [179]. An extensive comparison of pre-trained models established that they perform better than other deep learning and machine learning algorithms for classification tasks of lung cancer nodules using CT scans [180]. In addition, pre-trained models were shown to perform very differently on mammogram analysis and tumor detection [81], which further demonstrates the impact of the
model’s structure on feature extraction. For lung cancer detection, when combined with an SVM classifier, AlexNet has a higher specificity and sensitivity than GoogleNet [115]. In the case of WSI for breast cancer classification, AlexNet was found to outperform all previously reported results but required additional pre-processing steps [123].

Results also depend on the type of feature extracted before classification. Jain et al. compared multiple pre-trained models (VGG19, InceptionV3, InceptionResNetV2, ResNet50, Xception, and MobileNet) for skin cancer classification and found that Xception performed the best with a 90.48% accuracy [181]. Another comparison between pre-trained models (VGG19, ResNet50, Xception, DenseNet121, and EfficientNetB0) for skin cancer detection showed that EfficientNet was the most accurate with a 91.45% accuracy [182]. A combination of pre-trained models (ResNet-50, DenseNet-201, and DarkNet-53) was reported to enhance the diagnosis of skin cancers, as this combination succeeded in extracting both low-level and deep features [183]. Ensemble networks are also often used with pre-trained models by combining different models, with a combination of ResNet152 and VGG19 leading to an accuracy of 90% [184]. Furthermore, MCDM (multi-criteria analysis method), which combines entropy and PROMETHEE (preference ranking organization method for enrichment of evaluations), has led to optimal performance for ResNet101 on skin cancer detection [185]. The use of pre-trained models also comes with a limitation, as they often are CPU- or GPU-intensive to train and fine-tune [186, 187, 59, 188]. Furthermore, ensembles of pre-trained models, significantly improve the predictions’ accuracy, as shown for breast cancer [189]. However, it does so at an even greater computing cost.

3.5 Results

We summarize in Table 1 results obtained with CNN models for skin cancer [1, 70, 77, 165, 190, 191, 192, 193, 178, 188], lung cancer [107, 194, 195, 196, 197, 108, 198, 3] and breast cancer [55, 123, 199, 200, 201, 177, 184, 202, 203, 170, 204, 205]. Generally speaking, the CNN architecture is perfectly suited to obtain highly accurate results, with a 99% accuracy reported in recent work [128]. CNN models have been instrumental in determining common patterns in histology images across cancer types [206]. They can be useful for both binary and multi-classification tasks, as discussed in recent work highlighting the importance of binary decisions [31], and the challenges of multi-class predictions [207]. Deep learning algorithms can determine subtypes of cancers, a diagnosis that is often more complex to make for an expert than the binary choice between malignant and benign [187]. Casting a multi-class classification into a binary classification can often alleviate this issue [192]. Results on lung and colon cancer classification reveal that models that perform well in binary decisions can exhibit a decreased performance in multi-class classification [208].

Several studies have compared the performance of deep learning models with diagnoses made by specialists [55, 209] or conventional image analyzers [210]. A comparison of the predictions made by CNN models with diagnoses from dermatologists shows that the specificity and sensitivity of deep learning models are superior [1]. The impact of several technical parameters on CNN models was assessed systematically in recent work. For instance, the assessment of the JPEG compression of WSI was evaluated and demonstrated the robustness of CNN models [211]. The structure of the CNN network is also of great significance, as shown by Manikavasagam et al. who revealed that a five convolutional layer model leads to a 99% accuracy [3]. Fig. 3 shows the impact of the number of layers on several metrics, including accuracy, specificity, and sensitivity. This plot also indicates that the model performance does not correlate with its size. Most models lead to an accuracy greater than 0.70. In addition, Fig. 3 shows that the deep learning models considered here are either very large, with more than a hundred layers, or fairly small, with fewer than 50 layers. Comparisons between CNN and pre-trained models have shown that small CNN tailored for a given application can perform better than the pre-trained models [212]. As discussed in the previous section, this has led to the development of biomedically-oriented pre-trained models trained on databases other than ImageNet.
### Skin Cancer

| Reference | Database          | Accuracy       | Precision | Recall=Sensitivity | AUC  | F-score | Specificity |
|-----------|-------------------|----------------|-----------|--------------------|------|---------|-------------|
| [11]      | NA                |                |           | 0.823              |      |         |             |
| [77]      | ISBI              | 0.904          |           | 0.820              |      |         |             |
| [165]     | DermIS, Dermquest | 0.91           | 0.84      | 0.95               |      |         |             |
| [193]     | ISIC              | 0.75           | 0.77      | 0.73               | 0.75 | 0.75    | 0.78        |

### Lung Cancer

| Reference | Database          | Accuracy       | Precision | Recall=Sensitivity | AUC  | F-score | Specificity |
|-----------|-------------------|----------------|-----------|--------------------|------|---------|-------------|
| [13]      | LIDC/IDRI         | 0.9888         |           | 0.9962             | 0.928|         |             |
| [107]     | LIDC/IDRI         | 0.873          |           | 0.804              |      |         |             |
| [108]     | LIDC/IDRI         | 0.8879         |           | 0.94               |      |         |             |
| [194]     | NA                | 0.93           |           | 0.87               | 0.82 |         |             |
| [195]     | LIDC/IDRI         | 0.88           |           | up to 0.94         | 0.943|         |             |
| [196]     | LIDC              | 0.83           |           | 0.83               |      | 0.83    |             |
| [197]     | NA                | 0.90           |           | 0.92               | 0.94 |         |             |
| [198]     | LUNA16            | 0.844          |           | 0.844              |      |         |             |

### Breast Cancer

| Reference | Database          | Accuracy       | Precision | Recall=Sensitivity | AUC  | F-score | Specificity |
|-----------|-------------------|----------------|-----------|--------------------|------|---------|-------------|
| [55]      | NA                | 0.8105         | 0.7273    | 0.8136             | 0.8054|         |             |
| [123]     | ICPR-2012, MITOS-ATYPIA-2014 | 0.95 | 0.86 | 0.96 | 0.94 | 0.9435 | 0.9577 |
| [177]     | kaggle            | 0.85           | 0.92      | 0.8947             | 0.967|         |             |
| [204]     | NA                | 0.9751         | 0.9452    | 0.9925             | 0.859|         |             |
| [203]     | BreakHis, BC 2015 | 0.837          | 0.908     | 0.921              | 0.811| 0.863   |             |
| [201]     | ICPR              | 0.784          |           | 0.909              | 0.951|         |             |
| [199]     | NA                | 0.9524         | 0.9611    | 0.9503             |      |         |             |

Table 1: Summary of metrics reported for different CNN-based and pre-trained models for classification and detection of skin, lung and breast cancers. (a): Breast cancer challenge
Several studies have focused on developing alternative CNN architectures. Recurrent Residual Convolutional Neural Network (IRRCNN) models exhibit higher accuracy than patching-based CNN models when applied to histological images [203], and approaches leveraging wavelet decomposition techniques led to a higher AUC, of the order of 94% than conventional CNN models [213]. The YOLO algorithm was also recently used in cancer detection and classification of mammograms [214, 215]. Its combination with pre-trained models, such as ResNet50 for feature extraction, leads to high accuracy and an F1-score greater than 90% [215]. While algorithms identify larger tumors accurately, masses that are close to one another are often challenging to diagnose [214]. Additional models that fuse the wider context of information using multiscale filters provide accurate results for the classification of breast cancers, with a sensitivity of 96% and an AUC of 0.99, without increasing the computation time [216]. Similarly, radiomic-based models have drawn increased interest because of their ability to extract the most relevant features [217, 218]. Combinations of networks were recently developed, with an architecture composed of two independent artificial neural networks (ANNs), one feature constructor CNN, and one classification ANN. This led to the accurate identification of basal cell carcinoma in histological images [61]. Alternatively, deep residual neural networks, supplemented with transfer learning, allow for the differentiation of various lung cancer types from CT scans with up to 85% accuracy [219]. Deep residual neural network models are also used for cancer classification, especially when combined with SVM classifiers [186, 220].

Ensemble learning approaches are common techniques to improve the models’ prediction [221, 137, 2, 188]. When applied to breast cancer classification, ensembles of pre-trained models achieve up to 90%
accuracy [222]. Similarly, when combined with directed acyclic graphs, ensemble learning yields a 76.6% accuracy for the multi-class classification of dermoscopic images [192].

Several studies have also examined the potential of deep learning to obtain parallel information that leads to cancer diagnosis. For instance, the cancer stage correlates with the nodule size. Ohno et al. use CNNs to determine the change in nodule size in lung cancers [197]. Deep learning techniques can calculate the number of nuclei and quantify the spread of cancerous cells [223]. However, it is important to note that the accuracy reported in classification studies that require prior knowledge of the nodules’ position will likely decrease if both detection and classification tasks were carried out [196]. It illustrates the limitation of traditional CNN models and accounts for the recent development of segmentation and detection-based models.

CNN models also require large datasets with labeled images. Such datasets are often hard to access but are necessary to perform supervised learning. Thus, partly supervised or fully unsupervised techniques have recently been designed for cancer classification [163, 82]. The former focuses on semi-supervised networks and leads to a 92.53% accuracy. However, supervised learning has recently been reported to be more selective than unsupervised learning for lung nodule classification [22].

The choice of a specific dataset is often crucial and leads to significant accuracy differences (94.8% to 98.4% on skin cancers) [70]. Furthermore, methods were recently proposed to reduce the number of false positives [224] by removing non-relevant images with R-CNN models [225] and through the use of cascade models, with a detection step followed by a diagnosis step [139]. A drawback of the first approach is that it reduces the number of images in the database. While the second approach does not reduce the database size, it results in an increase in computing time. This is because two or more models are required, and this can become a significant issue for applications involving large databases [226]. Alternatively, combining the model’s prediction with physiological and clinical information can also lead to a reduction in the number of false positives [226]. Dual-path techniques for CNN (DualCoreNet) have shown promising results by combining segmentation and classification tasks [110]. Given the general scarcity of databases with labeled data, unsupervised learning methods are emerging, but have yet to become popular in the biomedical field [227, 201, 104].

Metrics, such as sensitivity and specificity rather than accuracy, allow for a direct comparison with diagnoses made by physicians [228]. As a result, studies are increasingly focusing on the improvement of specificity and sensitivity rather than accuracy [229, 226, 198, 89]. We add that other metrics such as the F2- and F3-score are also valuable to assess the model’s performance [2].

4 Conclusion

In this review, we discuss the tremendous, and ongoing, progress in applications of machine learning and deep learning for cancer detection and diagnosis. We focus primarily on the examples of medical images for lung, skin, and breast cancer detection. Here we examine the various steps involved in the building of a cancer prediction model, from the pre-processing of the data, the extraction of features, and the classification tasks. The application of machine learning and deep learning methods in the biomedical field is extremely bright. Comparisons between diagnoses made by pathologists and models’ predictions reveal that such models can lead to a higher diagnostic accuracy than specialists [230, 231, 232, 233]. However, this review also identifies several outstanding challenges. Model training is often limited to a single database and, as such, relies on a rather small number of images that originate from the same source and thus lack diversity [60, 174]. This means that generalization to unseen data remains a significant challenge [234]. Another widespread issue is the lack of public availability of datasets developed in-house [173]. Furthermore, ongoing efforts focus on improving the efficiency of segmentation and detection tasks [235, 104].

The applications of machine learning and deep learning algorithms extend well beyond the development of cancer prediction models in "simple" cases, i.e., when no other pathology can account for the symptoms. In
 recent work, DL models can classify and diagnose cancers, COVID-19, and pneumonia from chest X-rays and CT images [236]. Deep learning is now applied to uncover connections between histological images and multi-omic features [237]. Further insight can also be provided by applying deep learning to other types of data, including clinical studies [248], cancer-related diseases [65], actin fibers detection [239], volumetric data [235], as well as genetic information [240, 241, 242, 243]. Deep learning has also shown promising results in treatment prediction, risk prediction, and lab analysis [244, 245, 22]. Finally, the handling of personal data and medical history will require secure protocols. Protocols and software are currently under development for applications in a hospital setting [246], but also in the case of smartphone apps for skin cancer detection [247, 248].

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