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Computer-Aided Diagnosis of Cancer using Microscopic Imaging and AI Techniques – Review

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Abstract: This review explores the landscape of cancer growth detection methodologies utilizing microscopic images. It comprehensively examines diverse approaches, ranging from traditional image processing techniques to cutting-edge machine learning and deep learning algorithms. The review focuses the significance of various image features, including texture, shape, and color, in distinguishing cancerous growth from normal tissue. Emphasizing the need for tailored strategies for different cancer types, the review addresses challenges and opportunities in leveraging microscopic images for precise and early-stage cancer detection. By synthesizing insights from multiple studies, the review provides a holistic overview of the current state of cancer growth detection through microscopic imaging, contributing to the advancement of diagnostic tools and methodologies in oncology.

Keywords: Cancer, Growth detection, Microscopic images, Image processing, Machine learning, Deep learning

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Introduction

Cancer detection is a challenge that pathologists and other medical professionals have long faced in order to make diagnoses and develop treatment plans. Results of manual cancer identification from microscope pictures can vary from expert to expert due to variables like the subjective nature of the process and the lack of exact quantitative criteria to classify the microscopic images as malignant or benign. When feature-based algorithms are used, automated cancer cell detection from microscope pictures improves upon the previously noted issues and produces findings that are both clinically significant and biologically interpretable (Kumar *et al.*, 2015).

Cancer occurs when cells multiply uncontrolled and infect nearby tissues via the lymphatic and circulatory systems. In 2018, it was one of the primary reasons behind a significant number of deaths, accounting for 9.6 million fatalities and 18 million new cases (Bray *et al.*, 2018). About 70% of cancer-related fatalities take place in countries classified as low or middle-income countries. Environmental factors such as carcinogens, ultraviolet (UV) or radioactive (Ra) radiation and certain chemicals, as well as one's lifestyle and health state, such as tobacco, alcohol, and infections such as HIV and HPV, all contribute to the development of cancer. Each year, more than 330,000 individuals die from oral and pharyngeal cancers, whereas an estimated 657,000 more are diagnosed with these disorders (WHO, 2020). The high mortality rate of oral cancer is exacerbated by a lack of early identification. There could be a link between earlier cancer identification and improved patient survival rates (Loud and Murphy, 2017). Breast cancer stands as the most frequently identified cancer among female, while lung and prostate cancer are the most prevalent cancers detected in male. Extreme sun exposure, which causes skin cancer, is a major public health concern in hot-weather countries. Melanoma ranks as the most lethal form of skin cancer, whereas squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are less commonly found, they are equally dangerous and require timely identification for best treatment outcomes. Pathological study of tissue samples is the traditional method for diagnosing cancer. The catch is that this method necessitates the removal of tissue from possible problem areas before morphological abnormalities can be found (Santos *et al.*, 2017). The procedure takes a long time and is entirely at the discretion of the pathologist. Along with morphological and metabolic alterations, neoplastic tissue transformation occurs concurrently (Dudka *et al.*, 2020).

Types of Cancer Detectable with Microscopic Images:

Microscopic images have the potential to significantly improve the identification and diagnosis of many cancer forms. Using microscopic images, cancer detection and diagnosis are commonly achieved by the use of cell size and form, texture, morphology, and other visual indications (Kumar *et al.*, 2015).

(i) *Blood cancer*:

Leukemia is a malignant malignancy that predominantly impacts erythrocytes. The human bloodstream is predominantly composed of red blood cells, white blood cells, and platelets, all of which serve distinct functions. Plasma also makes up blood. The presence of white blood cells is critical for the immune system to effectively combat both malignancy and infection. Angiogenesis and hematocritric circulation are facilitated by red blood cells. The pivotal significance of platelets in the processes of blood coagulation and hemostasis is widely recognized (Valencio *et al.*, 2004). Many image processing algorithms that can detect blood cancer have been developed as a result of research into biomedical imaging of human blood samples. Certain strategies such as thresholding are employed in some of these systems to determine the blood cell ratio for cancer cell detection. In this study, the quantity of cancerous blood cells was measured through the use of microscopic imaging techniques (Fig. 1).

(ii) *Oral Cancer*:

Squamous cells in the soft tissues of the mouth, such as the tongue, cheeks, and lips, are the primary source of most oral malignancies (Epstein and Barasch, 2018). Malignant squamous cells are distinguished from normal ones by a marked difference in size and morphology upon microscopic examination (Fig. 2) (Ahmed *et al.*, 2019). The microscopic examination required for a conclusive diagnosis of oral cancer can only be performed by a highly skilled and experienced professional. Although algorithm-guided detection at the microscopic level holds promise for substantially alleviating the workload of specialists, its application in oral cancer diagnosis has been relatively underappreciated.

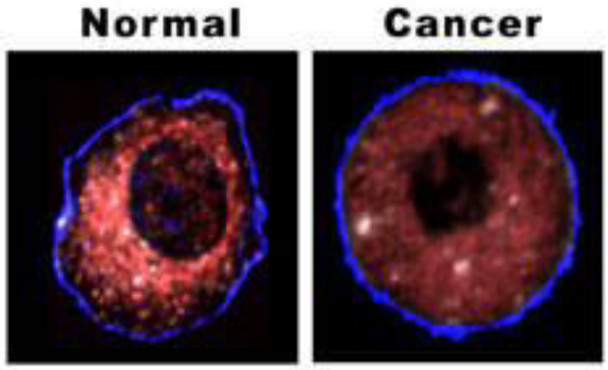

Fig. 1: Normal and Cancerous Cell. (Courtesy: https://newsreleases.sandia.gov/releases/2005/optics-lasers/biocavitylaser.html)

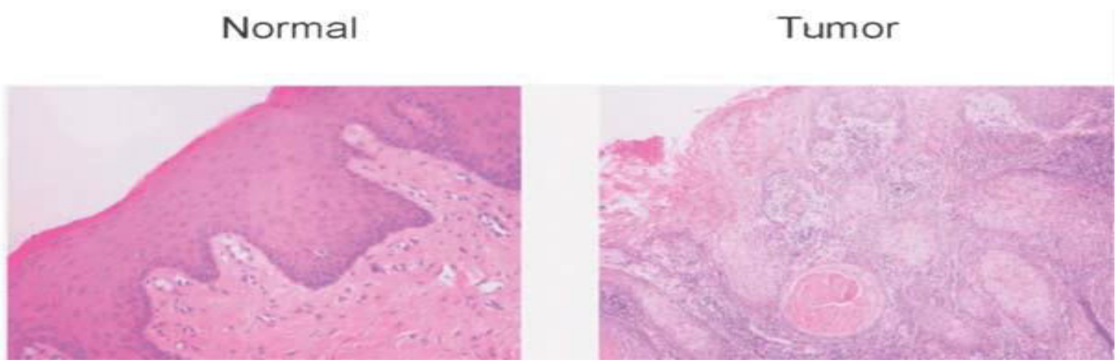

Fig. 2: Oral cavity normal and cancer cell. (Courtesy: https://www.nature.com/articles/sj.bdj.2018.926)

(iii) *Gastric cancer*:

One of the biggest concerns in the healthcare industry is the global prevalence of gastric cancer (Fig. 3). An imprudent approximation (De Martel *et al.*, 2012) attributes stomach cancer to *Helicobacter pylori* infection in 74.7% of non-cardia gastrointestinal malignancies, or 650 thousand cases each year. Nevertheless, the true proportion of these lesions associated with infections could be considerably greater. The Eurogast-EPIC study (González *et al.*, 2012) reported that *Helicobacter pylori* were identified in 93.2% of patients diagnosed with gastric cancer in Europe. In contrast, a mere 0.66 per cent of cancer patients in Japan exhibited no indications of infection.

Recent Advances in Microscopic Image-based Cancer Detection:

(a) *Cancer detection using machine learning*:

(i) *Brain tumor*:

A conglomeration of abnormal cells in four dimensions is known as a brain tumor. Generally, tumors graded 1 and 2 develop slowly, whereas grades 3 and 4 grow aggressively, presenting greater challenges for treatment. Achieving higher accuracy involves initially processing the input image to remove noise and non-brain tissues (Nazir *et al.*, 2019). This preprocessing step is crucial in diagnosing tumors. Techniques such as fuzzy C-means, k-means clustering, or the Otsu threshold method are commonly used for brain tumor segmentation. Currently, CNN architecture stands as an advanced method for identifying brain cancer. The process of segmenting the data, getting ready for deep learning training, and finally estimating the chance of cancer growth is depicted in Figure 4.

Iqbal and colleagues introduced a sophisti-

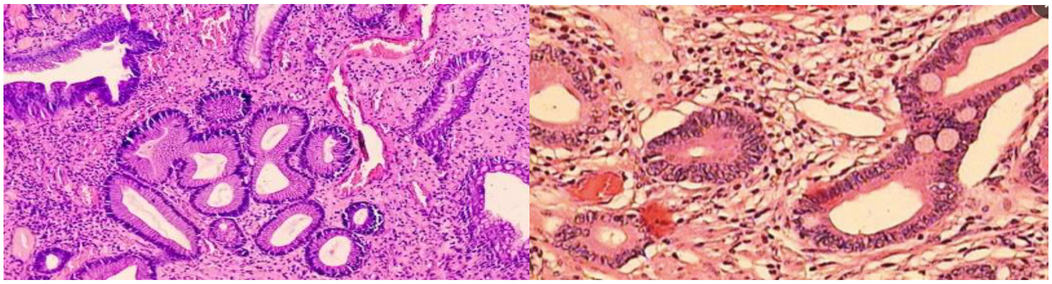

Fig. 3: Normal and cancer cell of gastric. Courtesy: https://www.researchgate.net/figure/Histology-of-the-tumor-invasive-region-in-human-OSCC-A-B-Representative-histological_fig3_323192623

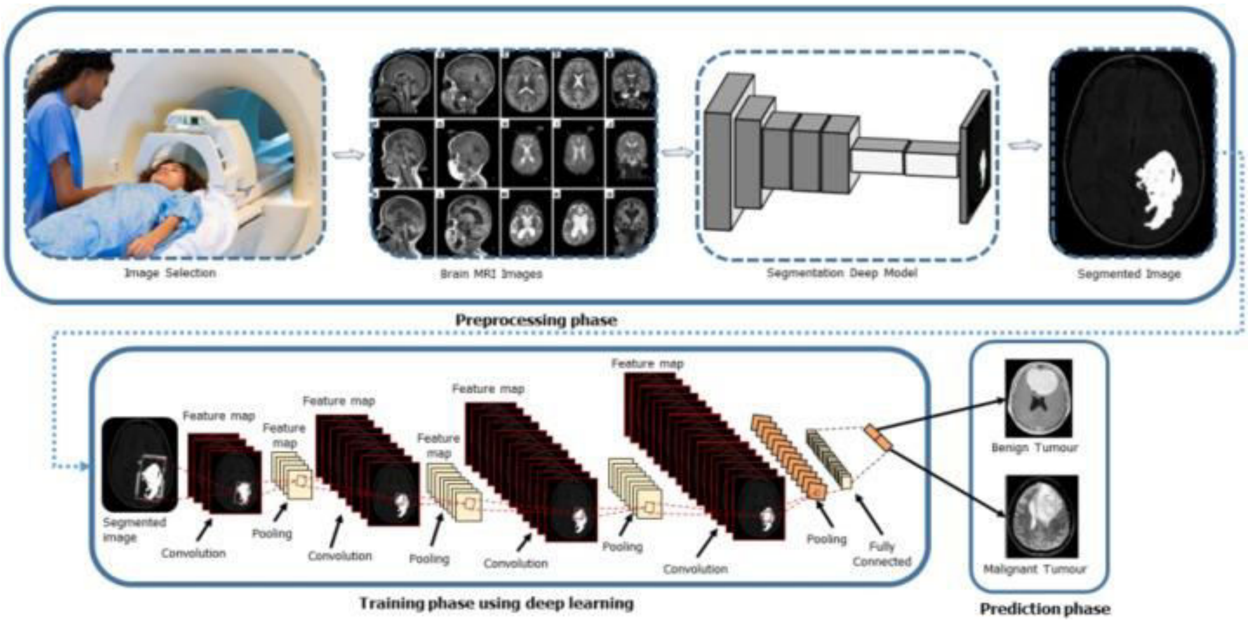

Fig. 4: Generalized framework for deep leaning-based brain tumor classification.

cated deep learning model that employs Medical Benchmarks, long short-term memory (LSTM), and convolutional neural networks (ConvNet) to achieve accurate brain tumor segmentation. Peak performance is achieved by combining ConvNet and LSTM, two separate models that are trained on the same dataset. They fused the two models. This explains why it is simple to obtain a data collection that includes MRI pictures from four different modalities: T1, T2, T1c, and FLAIR. One can obtain MICCAI BRATS 2015. Numerous adjustments are implemented, and the most effective variations in output are integrated into the preprocessing techniques, which include edge enhancement, histogram equalization, and noise reduction, in order to increase the clarity of the photos. Class weighting is one method used by current models to address the issue of class inequality. Every experiment's outcome is recorded, and the trained model is verified with information from the same collection of photos. ConvNet receives a single excellence score of 75%, an LSTM-based network receives 80%, and a total fusion of 82.29% is attained. The Grab cut technique (Saba *et al*., 2020) is efficiently employed to identify real loss symptoms from pseudo-symptoms while the Visual Geometry Transfer Learning System (VGG-19) is finalized to generate features that are then built (shape and texture) in series. Entropy developed these kinds of technologies in order to deliver fused vectors to classification units and recognize them with ease and accuracy. The model is assessed in the MICCAI challenge databases, such as the multi-modal brain tumour segmentation (BRATS) 2015, 2016, and 2017 databases, using cutting-edge scientific

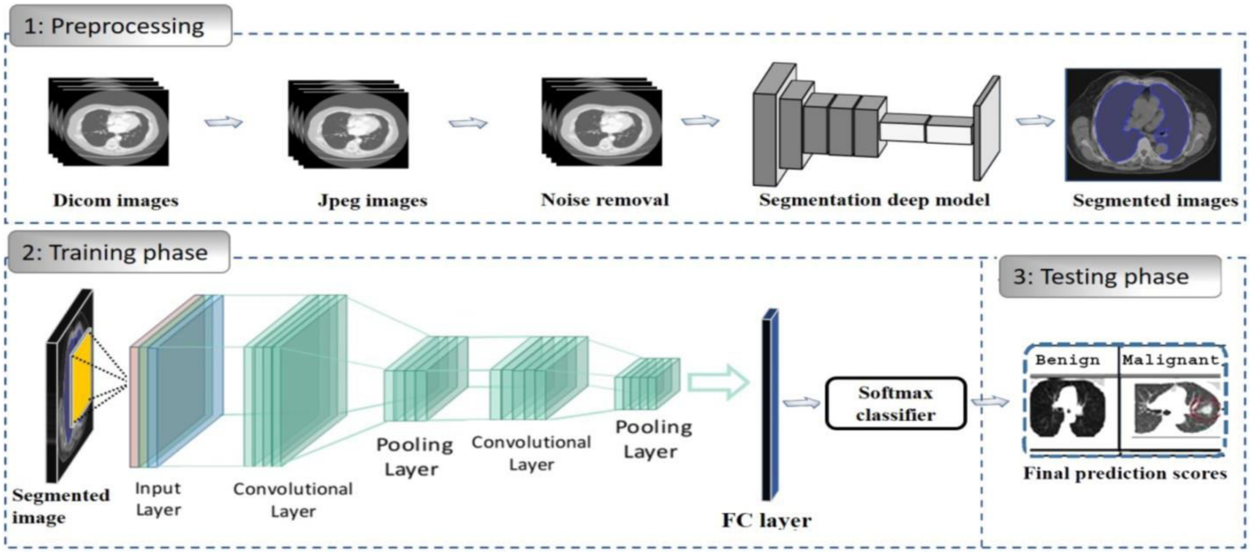

Fig. 5: Machine supported framework for lung nodules prediction.

image processing and computer-assisted intervention. The study includes results with a DSC of 0.99 using the 2015 BRATS, 1.00 using the 2016 BRATS, and 0.99 using the 2017 BRATS. By integrating their method with additional classifiers, the authors may have tested the method's viability, however they did not.

Mehmood *et al*. (2019) presented an efficient approach for brain imaging and modelling utilizing MR images. The brain and tumour regions are first separated from the MR sections using a semi-automated 3D segmentation technique. With a mean square error of 0.09, accuracy of 95.53%, sensitivity of 99.49%, precision of 99.0% and precision of 99.0%, it employs support vector machines (SVMs). Nonetheless, self-generated datasets were used for the testing. Das *et al.* (2019) were able to differentiate between sick and healthy tissue samples through the application of texture-based criteria. Eighty images of both sick and healthy tissue were selected from the GMCH, Guwahati Hospitals' archives. A collection of 172 feature vectors was produced using the five fusion descriptors-- The utilization of LBP, Tamura, HOG, GRLN, and GLCM involved feature extraction from images. Classifiers (SVM, K-NN, Logistic Regression, Quadratic Discriminant, Linear Discriminant) were applied to assess the collective and individual performance of each feature set. In the studies, combining these features resulted in an average classification accuracy boost to 98.6%, surpassing the accuracy achieved by using distinct feature sets and achieving a 100% accuracy rate.

A variety of brain regions were segmented (Ramzan *et al*., 2020) utilizing 3DCNN with substantial convolution and residual learning to assess the end-to-end mapping between voxel-level brain segments and MRI volumes. By aggregating data from three distinct sources, the average dice scores for three distinct brain regions were determined to be 0.879, while for nine components, they reached 0.914. In contrast to the previous study's average dice score of 0.876, the MRBrains18 data acquisition yielded a significantly higher average dice score of 0.903.

(ii) *Lung cancer*:

Lung cancer is one of the primary contributors to mortality worldwide among lung diseases. A number of percutaneous, surgical, and operative procedures may be beneficial for some patients with a small, dispersed tumour. Early lung nodule diagnosis and evaluation are made easier by applying machine learning to the interpretation of CT images produced by AI technologies. The procedures that decision support systems employ to review photos before categorizing them are depicted in Figure 5. Preprocessing, segmentation, feature extraction, and classification are some of these processes.

Shen *et al*. (2017) categorized lung nodules into "high suspicion" and "low suspicion" categories. Using a multi-crop convolution neural network and a new multi-crop pooling strategy, this method uses maximal pooling times and convolutional characteristic map region removal to extract meaningful information from nodules. They achieved good results with the LIDC-IDRI data by employing this method, including a classification precision of 87.14% and a CUP score of 0.93%. PyRadiomics proposed categorizing lung nodules as either benign or malignant, according to Van-Griethuysen *et al.* (2017). They used the publicly accessible LIDC data sets cohort and a Python technique to produce 3D slicer front-end code. A straightforward incremental approach was employed by Tahoces *et al*. (2019) to assess the three-dimensional geometry of the aortic lumen beginning with an initial contour within. For the mean DSC of 0.951, the tests of the proposed approach produced values greater than 0.928 for all sixteen CT cases with full datasets. The sixteen selected cases had a median distance of less than 0.9 mm. High-quality outcomes can be obtained in both frequent and unusual cases because to the excellent accuracy of the suggested remedy.

Xie *et al*. (2019) proposed the Ingeniously enhancing CT imaging by employing a 2D neural CNN to detect lung nodules automatically. Before identifying potential nodule placements, the Faster R-CNN configuration is optimized utilizing two area proposal networks and a deconvolution layer comprising three models, each of which can process one of three segment types. By doing so, a merged output can be generated. The next stage involves improving the 2D CNN architecture to develop a classifier that can differentiate between real nodules and possible ones. It is recommended to employ a pattern that increases the susceptibility of lung nodule identification during the retraining phase. Finally, the tests are collated and put to a group vote. The thorough testing of LUNA16 has a sensitivity of 86.42%. The accuracy of the false-positive decrease is 74.4% at 1/2 FPs/scan and 73.4% at 1/8 FPs/scan.

Jiang *et al.* (2017) proposed the use of multi-patches generated from the lung image of the Frangi filter for the diagnosis of lung nodules. A four-layer neural network model that combines two image classes to collect data from four channels for radiologists to diagnose nodules. With 4.7 false-positives per scan and 15.1 false-positives per sample, it was possible able to reach 80.06% sensitivity, or 94% of the target. On a sizable collection of image data, they discovered that applying the patch-based learning method in several groups enhanced performance and greatly decreased false positives. Naqi *et al*. (2019, 2020) presented a four-step method for locating and diagnosing nodules. The abstraction of the lung region starts with the optimal gray-threshold, which is determined by optimizing Darwinian particles. Next, as a novel candidate identification strategy, a parametric system centered on the spatial health of the nodules is added. To properly represent the nodule, in the next step we will build a hybrid geometrical texture description that includes 2D and 3D structural information. A fresh perspective was presented, emphasizing the stacked autoencoder and softmax, to counteract these false-positive outcomes. By leveraging information from the largest publicly accessible database and the Lung Image Database Collaboration, the suggested approach successfully decreased the occurrence of false positives to 2.8 per scan, all the while preserving an exceptionally encouraging sensitivity level of 95.6%. (Naqi *et al.*2019) introduced a methodology for mechanically identifying and categorizing nodules. A hybrid sensing methodology is employed to identify 3D nodules through the integration of 3D neighbourhood networking, the Active Contour Model (ACM), and spatial property-based principles. For each nodule nominee, an Oriented Gradient Histogram (PCA) and geometric texture are combined to form a hybrid feature vector, or HOG-PCA. Sorting is done by four distinct classifiers: SVM, Adaboost, Naive Bayesian, and one more. The process of

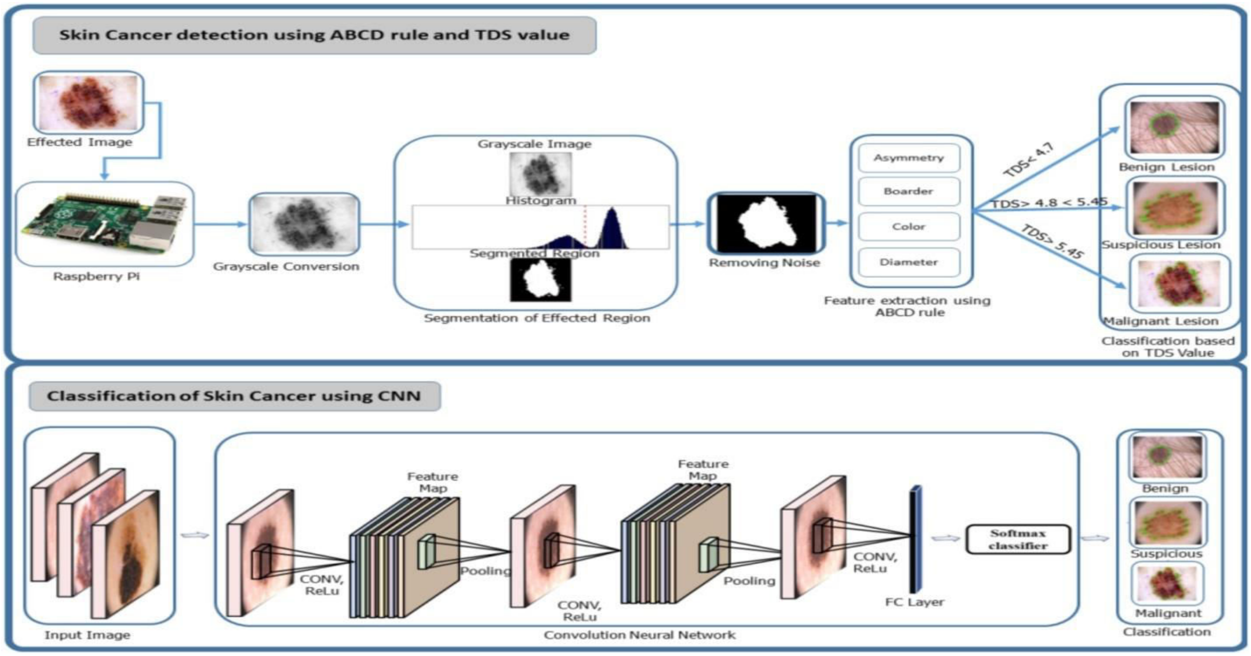

Fig. 6: Handcrafted and CNN feature extraction framework for skin cancer.

abstraction concludes with the presentation of the four distinct categories. In the evaluation, the exemplar provided by the Lung Image Database Consortium (LIDC) was utilized. AdaBoost has the highest scan rate, specificity, accuracy, and responsiveness when compared to other classifiers.

(iii) *Skin cancer*:

For several decades, dermatologists have been using machine-assisted methods to analyse dermoscopy images to help them make therapeutic decisions and spot highly dubious circumstances. In order to improve patient follow-up and undertake preliminary assessments, less experienced practitioners may also find value in utilizing intelligent technology as an extra tool (Barata *et al.*, 2018). The creation of machine learning techniques that can extract intricate features, such as the ABCD rule, a three-point checklist, is our main focus. Consequently, the field of medical imaging, which frequently uses deep convolutional neural networks (DCNNs) to manually generate features, witnessed impressive outcomes from these networks. Figure 6 illustrates the feature extraction framework utilizing both manual and CNN techniques.

Premaladha and Ravichandran (2016) introduced a highly developed approach to the categorization and forecasting of melanoma. By employing a contrast-limited adaptive histogram equalization configuration in conjunction with a median filter, this technique enhances the image. To differentiate skin lesions, a new segmentation method known as Normalized Otsu's Segmentation was used. This solved the issue of changing illumination. The thirteen features extracted from the segmented images were inputted into the proposed classifier, which is a neural network architecture that integrates deep learning and AdaBoost SVM. During the validation and testing phase, the system obtained a classification accuracy of 93% by utilizing an estimated 992 images of benign and malignant tumours.

The method provided by Bareiro Paniagua *et al*. (2016) for determining whether a lesion is malignant or benign is applied to a dermoscopy image. Classification, lesion segmentation, feature extraction from lesions, and image preprocessing were some of the modules comprising this method. In the pre-processing phase, eliminate any superfluous components, including filaments.

Feature extraction was performed using the ABCD rule on the previously segmented regions that were impacted.SVM was subsequently applied to ascertain whether the lesions were malignant or benign. Upon application to a dataset consisting of 104 dermoscopy images, the proposed method demonstrated experimental results indicating a sensitivity of 95% and a specificity of 83.33% with a precision of 90.63%. These results, in contrast to the diagnostic efficacy of traditional methods, indicate promise for the field of dermatology.

Khan *et al*. (2019) used features that are commonly used for image analysis, like colour and texture. Because these techniques primarily relied on manually created features, the machine-assisted framework's efficiency was undermined. Aima and Sharma (2019) tested CNN for early-stage melanoma skin cancer diagnosis using 514 dermoscopy images from the ISIC dataset, which is consistent with this. They were 74.76% accurate and had a validation loss of 57.56%. An inference model for skin cancer based on 10,015 pre-trained smartphone images was reported by Dai et al. (2019) in their study. Due to local storage of the test data, all computations for assessing a new input were performed there. Yet, their approach improved privacy, saved electricity, and decreased latency with 75.2% model accuracy. Relative to the published works, the stated precision is substantially lower. Saba *et al.* (2020) proposed a DCNN-based automated technique for the detection and recognition of cutaneous lesions consisting of three stages: enhancement of contrast, extraction of lesion boundaries, and extraction of in-depth features. In order to select discriminant features, the entropy technique was implemented. An evaluation of the proposed method is conducted utilizing the ISIC 2017 and PH2 datasets. Furthermore, the validation process for the recognition phase incorporates the ISBI 2016 and 2017 datasets. With accuracy rates of 94.8%, 95.1%, and 94.4% for the ISBI 2017 dataset, PH2 dataset, and ISBI dataset, respectively, the authors assert that their methodology exhibited superior performance to established methodologies.

(b) *Cancer detection using Deep Learning Technique*:

(i) *Lung cancer*:

Numerous investigations have been undertaken on diverse imaging modalities since the advent of deep learning with the objective of lung cancer detection and diagnosis. From pathology images of lung cancer, Zhu *et al*. (2016) employed DCNNs to predict survival periods for patients. By employing a trainable multi-view deep CNN model and utilizing 3D computed tomography (CT) data, Hussein *et al.* (2017) introduced a nodule classification method. A median intensity projection was employed to generate a single two-dimensional region for each dimension before the CNN model commenced its training. In order to construct a 3D tensor, we then linked the patches. An additional deep CNN model with multiple views, which classifies nodules using 3D CT scans, was suggested by Setio *et al*. (2016). Prior to dividing it into 2D patches, their model produced a 3D image. For the purpose of extracting features, they next fed each 2D patch into a different CNN model. A combined collection of retrieved attributes was ultimately provided to the classifiers (Dou *et al*., 2016). The 3D convolutional neural network in order to discover information directly from 3D CT scans, as opposed to constructing 2D regions for CNN model training. Using a multilayer model, the problem of nodule size variation was addressed. The multi-crop convolutional neural network (MC-CNN) was introduced by Shen *et al*. (2017) as a feasible resolution to the challenge posed by significant size variability in nodule classification.MC-CNNs implemented a multi-crop pooling strategy (Shen *et al*., 2017) as opposed to the traditional maximum pooling method utilized by CNN models in order to generate features at different dimensions.

Wang *et al*. (2017) stated that there is a potential for erroneous classification outcomes due to the identification of extraneous data concerning a pulmonary nodule by a deep learning model. Given this, their recommendation was to identify lung nodules by merging 26 hand-crafted features with the deep data that a CNN model retrieved (Tajbakhsh and Suzuki, 2017). The effectiveness of massive-training artificial neural networks (MTANNs) and CNNs in identifying and differentiating pulmonary nodules in CT images was evaluated in a study. Large datasets and small datasets were the two training approaches used in the study. Even when CNN models' performance was improved with smaller training datasets, the findings of his research showed that MTANNs outperformed CNNs.

(ii) *Skin cancer*:

Common skin malignancies have sparked new efforts to employ deep learning to develop algorithms that can aid in disease identification. (Esteva *et al.*, 2017) utilized a massive dataset of 129,450 clinical images to evaluate the classify-cation performance of pre-trained CNNs for cutaneous cancer. Mahbod *et al*. (2019) employed pre-trained CNNs to classify skin lesions. Majtner *et al*. (2016) reported an approach for melanoma identification that combines deep characteristics with hand-crafted ones. To calculate probability scores, we employed two support vector machine (SVM) classifiers: one trained on features recovered from grayscale images using a CNN model, and the other trained on features taken from raw colour images using R Surf and local binary patterns (LBPs). The final result was generated from the classifier with the highest score.

Dermoscopy images were utilized to identify regular globules and typical networks through the proposed use of deep CNNs (Demyanov *et al*., 2016). The CNN was trained in accordance with the recommended methodology utilizing the industry-standard stochastic gradient descent algorithm. Yu *et al*. (2016) proposed Melanoma detection through the utilization of deep residual layers on dermoscopy images. There were two networks in the recommended system. Fully convolutional residual networks (FCRNs) were one possibility; they differed from FCNs in that they employed residual blocks instead of common convolutional layers. The dermoscopy image was segmented using a score map created by this system. Following that, the skin lesion-containing region was reduced and cropped before being classified using a deep residual network.

(iii) *Brain cancer*:

Brain tumours are solid, uncontrollably growing growths that can originate in any area of the brain. The diagnostic and detection capabilities of deep learning applications in brain cancer have been the subject of numerous studies. Deep learning is investigated by (Gao *et al*., 2017) through the examination of CT brain images for tumour cell categorization. To train a 2D CNN and a 3D CNN independently, the technique initially employed slice images of 2D and 3D images, respectively. By combining the outputs of the two CNNs, the final prediction result was obtained. The technique that was suggested demonstrated superior perfor-mance compared to alternative methods that utilized the KAZE feature and the 2D and 3D scale-invariant feature transform (SIFT), according to (Alcantarilla *et al*., 2012). Automatic segmentation of MR images was introduced by using a CNN-based approach. The intensity normalization and enhancement for brain tumour segmentation were examined in the proposed method. Havaei *et al.* (2017) cited a plethora of pertinent research in their presentation of a CNN model for an MR image-based brain tumour segmentation technique. The final convolutional layers, which were proposed as fully linked layers, significantly accelerated the process while also integrating local and global contextual input. A novel method for segmenting brain tumours was developed by Zhao *et al.* (2018) by fusing FCNs with conditional random fields (CRFs). The recommended method was used to train the FCN and CRF first using picture patches. Subsequently, image fragments were promptly employed to refine the overall structure. Pertaining to the segmentation of brain lesions, Kamnitsas *et al.* (2017) suggested a deep three-dimensional convolutional neural network (CNN).

The performance of deep CNNs was

investigated by Paredes *et al*. (2017) in relation to various training image datasets. The two universities collected the datasets using various imaging devices, contrast methods, or patient populations. For their MRI investigations, patients with glioblastoma (GBM) acted as test subjects and experiment subjects. half the time, data from the same institution or another was used to evaluate the CNN (Milletari *et al.*, 2016). The same organization provided the data for training. The approach assumed that the training and testing sets would always have the same size. Their investigations revealed that the test's accuracy at one institution was higher than its accuracy at another.

Significance of the Study:

By virtue of its implementation of microscopic images, this study contributes significantly to the development of cancer diagnostics. By conducting an extensive examination of various approaches, such as traditional image processing and cutting-edge machine learning, this research successfully addresses an urgent need for accurate and prompt detection of various types of cancer. The findings not only shed light on the nuances of distinguishing cancerous growth from normal tissue but also emphasize the importance of tailored approaches for different cancers. Ultimately, the study's insights have practical implications in the development of more effective diagnostic tools for clinicians, paving the way for timely interventions, personalized treatment strategies, and improved patient outcomes in the challenging landscape of cancer detection and management.

Conclusion

In conclusion, the diverse approaches explored in the realm of cancer growth detection using microscopic images showcase a promising trajectory for advancing diagnostic capabilities. Profound advancements have been made in improving accuracy and efficiency through the incorporation of cutting-edge machine learning algorithms with image processing techniques. While challenges persist, particularly in tailoring methodologies to specific cancer types, the synthesis of findings from various studies underscores the potential for robust and early-stage detection. The continued collaboration between researchers and clinicians, coupled with advancements in technology, holds the key to further refining and implementing these detection strategies in clinical settings, ultimately contributing to improved outcomes in cancer diagnosis and treatment.

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