

# Unleashing the Potential: Evolution of AI in the Detection of Cancer

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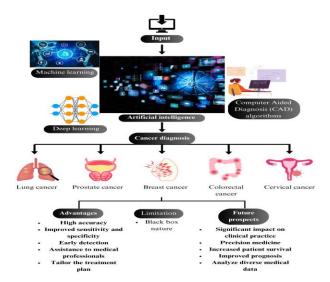
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#### **ABSTRACT**

Cancer, characterized by its rapid progression and high mortality rates, requires early detection and immediate intervention. Recent advancements in computer engineering and statistics, notably through AI (Artificial Intelligence), and machine learning, have revolutionized disease analysis. These technologies provide potent algorithms and predictive models, reshaping clinical cancer research and refining detection and management approaches. Consequently, they bolster patient survival rates and therapeutic outcomes, marking a significant shift in our fight against this lethal disease. The following review thoroughly examines the significance of AI in cancer diagnosis and prognosis, exploring its benefits and drawbacks in depth. The article focuses on the tremendous accuracy of AI technology in predicting cancer, highlighting how it has revolutionized cancer research by breaking new ground. Additionally, the review delves into the various practical challenges and opportunities that need to be addressed while implementing AI in cancer healthcare settings. This comprehensive analysis aims to provide a detailed understanding of the benefits and boundaries of AI in cancer healthcare and its prospects. AI has the potential to transform cancer diagnosis and prognosis, improving patient outcomes and enabling a more efficient, patient-centered approach to treatment.

**Keywords**: Artificial intelligence; cancer diagnosis tools; machine learning; deep learning; AI software.

#### **GRAPHICAL ABSTRACT**





#### INTRODUCTION

Cancer is a major health issue that agonies millions of persons worldwide. Interpreting the data from 2018, there were 17 million reported cases of cancer globally [1]. The number of newly diagnosed cases has been increasing, with 19 million reported in 2020 alone with 10 million deaths [2]. In high-income countries like the US, approximately 1.7 million people suffered from the disease in 2019, while in the UK, the disease affected nearly half of the population aged 50 or above [1], [3]. Due to the rising incidence and mortality rates, it has become increasingly important to develop new tools and treatments that can improve survival rates. Some promising approaches include tumor adjuvant therapy and robotic surgery [4]. Despite the advancements in medical tools and technology, achieving satisfactory curative results for each individual remains a challenge. This is due to the uncertainty in the precision of diagnosis, which increases the need for optimal prognosis [5]. Accurately predicting the course of a disease would enable doctors and clinicians to plan appropriate treatments that eliminate the mental and physical hardships faced by patients.

Unfortunately, current approaches such as TNM (tumor, node, and metastasis) staging are not always accurate, which is why the art of AI technology has become increasingly important. Although developing AI algorithms that improve the accuracy of disease prediction has been challenging for engineers and scientists, it has been successfully established using conventional logistic regression and multi-factorial analysis. This has enabled the accurate prediction of the stage of the disease and the susceptibility of patients to the disease (Table 1). The integration of AI with bioinformatics tools has proved to be more effective than traditional statistical analysis methods, as demonstrated by various scientists [6], [7].

Within the realm of AI, that involves machine learning (ML) is one of its key components. ML essentially deals with the development of algorithms that can generate solutions without the need for explicit programming. It uses computational algorithms to train prediction models with large datasets. There are different types of ML models such as supervised, unsupervised, semi-supervised, and reinforcement learning. Supervised learning is a type of ML model that involves the use of a labeled dataset, where the algorithm is trained to identify patterns and relationships between inputs and their respective outputs. This type of model is commonly used for detecting nodules, characterizing nodules, and predicting cancer risk and survival rate. In contrast, unsupervised learning is a type of ML model that does not require a labeled dataset. Instead, it uses clustering algorithms to group similar inputs and identify connections between them. For example, unsupervised learning can be used for detecting oncogenes in cancer. Semi-supervised learning is a combination of both supervised and unsupervised learning, where the algorithm is trained on a partially labeled dataset. This type of model is useful when there is limited labeled data available. Reinforcement learning is another type of ML model that involves a reward function. The algorithm learns through trial and error by interacting with an environment (input) to maximize its reward and has appeared as an impressive tool for predicting the onset of diseases [8], [9]. By enhancing the fundamental aspects of early diagnosis and prognosis in cancer research, the accuracy of survival, recurrence, and susceptibility, ML has emerged as a valuable asset in the fight against cancer [10], [11], [12], [13], [14]. One of the subgroups of AI, known as Deep Learning (DL), consists of computer models that can obtain information from images in a way that is similar to how humans process visual information [15]. DL, a relatively new and emerging branch of ML, uses artificial neural networks to process images and reduce them to a set of numerical values that represent features. DL algorithms have been tested in various medical specialties and have been found to perform at levels comparable to human experts.



Radiomics, on the other hand, involves a technique that extracts quantitative data from an image. This demonstrates the potential of AI in transforming the medical field and improving patient outcomes [15]. This review highlights the promising role of AI in the early revealing and diagnosis of various types of cancer, which can potentially improve patient outcomes. In light of this, researchers in bioinformatics and the biomedical field are now designing tools that can improve the prediction of cancer prognosis and ultimately contribute to better treatment outcomes. It has been observed that the AI's practicality is notably heightened in the realm of diagnosis, owing to its capacity to analyze extensive datasets and large sample sizes efficiently.

Table 1. Application of AI Techniques in the Diagnosis of Different Carcinomas

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AI Technology	Methodology	Type of Cancer Detection	References
Lunit INSIGHT CXR	DL algorithm	Lung cancer	[16]
Aidence	Computer Aided Diagnosis algorithms (CAD)	Lung cancer	[17]
Siemen Healthineers AI-Rad Companion Chest CT	DL algorithm	Lung cancer	[18]
Zebra Medical Vision	ML and DL Algorithms	Lung cancer	[17]
Paige Prostate	ML Algorithm	Prostate cancer	[19]
Path AI	DL Algorithm	Prostate cancer	[20]
Tempus	ML and DL Algorithms	Prostate cancer	[21]
Prostate.ai	ML and DL Algorithms	Prostate cancer	[22]
Transpara	DL Algorithm	Breast cancer	[23], [24]
Volpara Density	ML Algorithm	Breast cancer	[25]
DM-Density	ML Algorithm	Breast cancer	[25]
QuantX	CADx Software	Breast cancer	[26]
Mia	DL Technology	Breast cancer	[27]
GI Genius	DL Algorithm	Colorectal cancer	[28]
SKOUT	CADe Module	Colorectal cancer	[29]
Advance Map-Based Superpixel Segmentation (AMBSS)	Quasi-newton-based Feed Forward Neural Network and Deep auto-encoder-based Extreme Learning Machine	Cervical cancer	[30]

## AI TECHNIQUES FOR DIAGNOSING DIFFERENT CARCINOMAS

## **Application of AI tools in Breast Cancer Detection**

Breast cancer persists as a complex and globally daunting public health concern. With approximately 2.3 million new cases detected worldwide, it represents nearly one-fourth of all female cancer diagnoses [31]. Studies indicate that this number could rise to 3 million by 2040 [32]. Gene expression profiling has categorized breast cancer into five subtypes: luminal A, luminal B, HER2-overexpressing, basal-like breast cancers (BLBC), and normal-like tumors. These intrinsic subtypes show variability in terms of morphological and pathological features, thereby differing in response to treatment [33]. Its high incidence rate and heterogenicity burden the healthcare system, as early detection and treatment are beneficial in improving a patient's prognosis. Mammography-based screening programs have been accepted and adopted due to their ability to reduce mortality rates. They are used as a



diagnostic tool and also help in determining the staging of breast cancer and assessing the efficacy of chemotherapy. Radiologists visually interpret mammographic images and may be prone to errors due to external or internal factors like an immense workload or abnormally high noise in the image. Integrating AI into breast cancer screening and diagnosis is essential to prevent human errors and ensure accurate early detection. Breast cancer imaging relies heavily on the fundamental aspects of AI, including ML, DL, and radiomics [18]. By applying these AI principles, it can greatly improve accuracy and efficiency in detecting and diagnosing breast cancer (figure 1) [34].

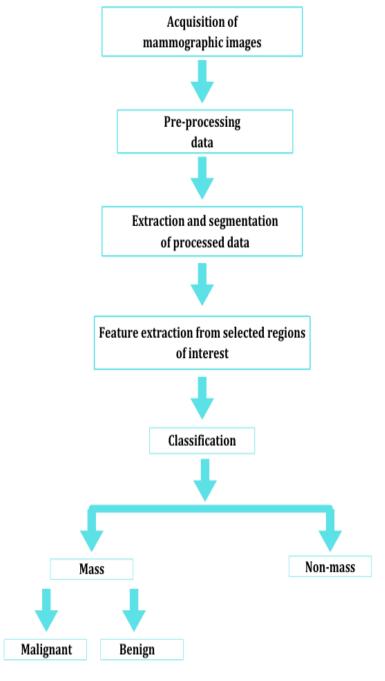


Fig. 1. AI in Breast Cancer Diagnosis.



The following AI tools are widely employed to precisely identify and diagnose breast cancer. For example: Screen Point Medical - Transpara Screen Point Medical developed an evidence-based AI software, Transpara, for breast cancer detection in mammograms. It initially previews and applies DL techniques to the digital mammogram, after which it categorizes potential abnormalities based on their probability of being malignant. The tool then provides an examination-based score, which can assist radiologists in their diagnoses. A study applied Transpara (version 1.3.0) to a data set of 240 mammographic images, which were reviewed by fourteen radiologists from centers in the US demonstrated improved breast cancer detection without an increase in reading time [23]. Michiro et al. compared the detection performance of the AI tool and three unaided human readers (HR) in a population of Japanese women. The AUC was higher for HR, and statistically, the diagnostic performance of Transpara was lower. Yet, the study suggested that developments in AI are expected to reduce the gap between computer and human evaluation [24]. A few other examples of diagnostic tools for breast cancer are- Volpara Solutions - Volpara Density<sup>TM</sup> and Densitas – DM-Density: A higher breast density score correlates with a higher risk of breast cancer. However, visual assessment of breast density is plagued by difficulties, such as high interobserver variability and abnormally high noise or masking in images of significantly dense breast tissues. This has led to the development of various AI tools for automated breast density assessment. Volpara Solutions developed an FDA-approved multivendor breast imaging software, VolapraDensity. It calculates volumetric breast density by extracting the thickness of fat and fibroglandular tissues in the mammogram [25]. In 2018, Densitas received FDA clearance for DM-Density, an ML-based breast density software that processes digital mammograms and computes breast density scores compatible with the BI-RADS system. These tools aid in the standardization of gauging mammographic density and enhance productivity by reducing diagnosis time. **Qlarity Imaging – QuantX<sup>TM</sup>:** When mammograms provide inconclusive data, MRI offers to be an advantageous alternative. QuantX<sup>TM</sup> is an FDA-approved CADx software developed by Qlarity Imaging (QI). It is indicated for evaluating breast abnormalities using MRI input. On processing user-selected regions of interest, it yields a QI score. This score aids radiologists in determining the presence of malignancy. Through a retrospective study, Jiang et al. determined that the application of QuantX<sup>TM</sup> performance in distinguishing cancerous breast lesions exhibited an increase in the average AUC of all readers from 0.71 to 0.76 (P = 0.04) through the software [26]. Kheiron Medical - Mia®: Mia, which stands for Mammography Intelligent Assessment, is an algorithm developed by Kheiron Medical. It provides suggestions for recall, behaves as an independent second reader, and highlights atypical breast tissue regions. In a three-phase study, researchers assessed its effectiveness as an adjunct reader in conjunction with standard double reading. Results demonstrated that it was capable of identifying infiltrative (83.3%) and minute ( $\leq 10$  mm, 47.0%) malignancies, suggesting that its application can improve the early detection of cancer [27].

**Mammography**: Mammography is a non-invasive method that has proven to be highly reliable in detecting early signs of breast cancer. According to a randomized control trial conducted by Duffy S et al., regular mammographic screening was offered to women aged between 40 to 49, which resulted in a 25% reduction in deaths caused by breast cancer during the first 10 years of the trial. The study also revealed that there was a further decrease in mortality rates on follow-up after an average of 23 years [35]. It produces high-resolution images of the breast tissue using low-energy X-rays. These images are then analyzed using AI to detect and classify non-palpable breast masses, calcifications, and breast density, and assess breast cancer risk. AI-powered mammography is also used to monitor patient response



to chemotherapy, thereby enabling doctors to make informed decisions regarding the most suitable treatment plan for their patients. Overall, mammography combined with AI analysis has proven to be an effective and harmless screening technique for breast cancer, helping to detect the disease in its early stages and improving patient outcomes.

**Breast Mass:** Breast masses are a common occurrence in breast cancer patients and are often identified through mammography. However, distinguishing these masses from normal breast tissue in mammographic images can be a challenging and time-consuming task. This is where computer-aided diagnosis (CAD) comes in as a crucial step in the diagnosis process. To tackle this challenge, S. Parvathavarthini et al. introduced a Crow search optimization-based Intuitionistic fuzzy clustering method with neighborhood attraction (CrSA-IFCM-NA) to pinpoint the region of interest. Demonstrating high efficacy in distinguishing masses, this approach serves as a valuable tool for radiologists in breast cancer diagnosis [36].

Calcifications: Breast calcifications are depositions of calcium oxalate or calcium phosphate. They are classified as macro- and microcalcifications. Macrocalcifications are observed as large, well-defined, diffused white spots on a mammogram that are often non-cancerous. Microcalcifications are  $\leq 0.1$  mm in size and may be an early sign of breast cancer, making them an essential component of CAD. Currently, several CAD systems can detect microcalcification clusters (MCs). Guo Y et al. proposed using a non-linking, simplified pulse-coupled neural network to detect MCs. Results showed a higher specificity of 94.7%, sensitivity of 96.3%, and accuracy of 95.8% [37].

Breast Density: Breast density (BD) is a crucial factor that increases the risk of breast cancer. The Breast Imaging Reporting & Data System (BI-RADS) categorizes breast density into four categories: predominantly fat, scattered fibroglandular densities, heterogeneously dense, and extremely dense. Research indicates that women with dense breast tissue, classified as BI-RADS density dense tissue, classified as BI-RADS density b [38]. To accurately determine breast density, DL algorithms that use convolutional neural networks have been developed, and they have shown high accuracy. One such algorithm, developed by Magni et al., achieved 89% accuracy in identifying non-dense and dense breasts, with 90% compliance with three independent radiologists [39]. Therefore, AI can be implemented to assess mammographic BD, significantly reducing the variability among radiologists and improving breast cancer prediction.

Breast Assessment Risk: Assessing the risk of breast cancer in an individual is crucial for early detection and effective treatment. The Gail model (BCRAT), the Breast Cancer Surveillance Consortium model (BCSC), the Tyrer-Cuzick model (IBIS), and the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm model (BOADICEA) are some of the widely used tools to evaluate the risk of breast cancer in an individual. These models require input, including (but not limited to age), age of menarche and menopause, number of offspring, breast density, family history, genetic profile, previous biopsies, race, ethnicity, and BMI. The models use a combination of the provided factors to calculate the 5-year, 10-year, or lifetime risk of breast cancer. Despite their widespread use, these models have their limitations, which include the lack of consideration of some essential factors and inaccuracies in some instances. However, AI-powered models have been considered advantageous when evaluating the risk of breast cancer. An exemplary model, Mirai, a mammography-based risk assessment tool, underwent rigorous testing and validation



across seven hospitals spanning five countries, including the USA, Israel, Sweden, Taiwan, and Brazil [40]. Mirai consistently demonstrated precision in predicting breast cancer risk over one to five years, indicating AI's potential to enhance detection. This technology offers a thorough and precise evaluation of individual breast cancer risk, promising improved diagnosis and treatment. Consequently, AI-driven models like Mirai hold promise for revolutionizing breast cancer screening, emerging as pivotal tools in the battle against this disease.

**Neoadjuvant Chemotherapy:** Neoadjuvant chemotherapy (NAC) stands out as an effective strategy for advanced cancer treatment. In a recent study led by Zhang, Kun et al., a novel method for predicting patients' pathological complete response (pCR) post-NAC was introduced. This involved developing and validating a contrast-enhanced spectral mammography (CESM)-based radiomics program tailored to anticipate pCR likelihood in individuals with locally advanced breast cancer. Encouragingly, the results showcased promising intra- and inter-observer ICCs ranging from 0.769 to 0.815 and 0.786 to 0.853, respectively. Moreover, the radiomics nomogram exhibited favorable calibration and discrimination performance. The study concluded that this innovative approach holds significant clinical promise in predicting pCR post-NAC for breast cancer patients [41].

## Application of AI Tools in Lung Cancer Detection

Lung cancer ranks among the most prevalent cancers globally after breast cancer and prostate cancer in females and males, respectively. It gauges approximately 2 million diagnoses and leads to around 1.8 million deaths [42]. Lung cancer in the early stages is not accurately distinguished as it is usually asymptomatic. It consists of a high morbidity and mortality rate since in most cases the diagnosis is done in the late stages [43]. In addition, the wide array of imaging features and histopathology makes it difficult for pathologists to choose the appropriate therapy. The clinical features range from a small single nodule to multiple nodules, pleural effusion, ground-glass opacity to multiple opacities, and lung collapse [15]. It is broadly classified into Non-small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC). NSCLC is the most common (85-90%) and is further classified into adenocarcinoma, squamous cell carcinoma, and large cell carcinoma [44]. As lung cancer is accurately diagnosed after the onset of symptoms (in the end stage), it results in a poor prognosis. The diversity of lung cancer makes it a prime subject for integrating AI and its use can help in diagnosing the disease in the remediable stage.

The following AI tools are extensively used in combination with radiographical imaging for the absolute identification and diagnosis of lung cancer. Such as **Lunit INSIGHT CXR-** It is a deep learning (DL) algorithm that is used following a chest CT for accurate diagnosis of lung cancer, and detection of other pulmonary abnormalities. It can be compared to the role of an expert radiologist in the detection of abnormalities and improves the accuracy of the diagnosis [16]. **Aidence-** It is a computer-aided diagnosis (CAD) model that is also helpful in properly detecting suspicious tumors, their characterization, and predicting the growth pattern of cancer. It can help chest radiologists in the proper identification of nodules and has been proven to be used routinely in the clinical setting [17]. **Siemens Healthineers AI-Rad Companion Chest CT** - It is another type of AI model specifically DL specializing in aiding expert radiologists in detecting cancerous nodules, their classification, and segmentation [18]. **Zebra Medical Vision-** is another company that has created models or algorithms that are used along with radiological tests such as X-rays or CT scans to derive a proper diagnosis [17]. All of these tools have been proven effective in enhancing the specificity and sensitivity



of nodule detection, segmentation, and differentiation in thoracic radiological examinations. Therefore, they are used as a second reader during the screening or diagnosis of cancer leading to decreased false positive and negative rates and faster results (figure 2) [45].

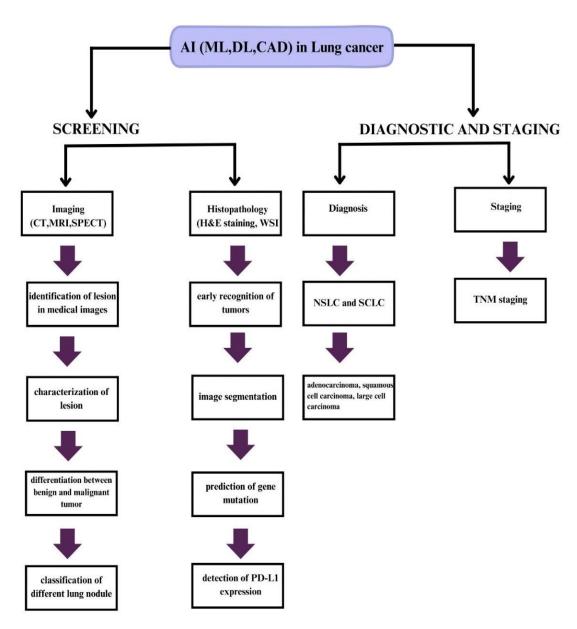


Fig. 2. AI Techniques in Lung Cancer Detection.

**CAD System:** Recent advances in AI-based techniques and CAD systems have greatly improved the accuracy of lung cancer diagnosis and screening (figure 2). By using sophisticated algorithms and machine learning, these systems can help radiologists detect lesions and nodules that might otherwise be missed. These systems have been shown to increase the sensitivity of radiologists from 65.1% to 70.3% while reducing the false negative rate from 0.2% to 0.18% [15] CAD systems can be divided into two main categories: computer-aided detection (CADe) and computer-aided diagnosis (CADx). CADe systems help locate lesions and nodules in medical images, while CADx systems are effective at characterizing these structures and determining whether they are benign or malignant.



**Homogenizing CAD Systems:** The latest example of CAD is Homogenizing CAD systems with screening tests such as Chest X-ray (CXR) and Chest CT have been proven to be highly beneficial. By incorporating radiomics, medical images can be computed using mathematical formulations that help convert the area of interest into a larger dimension of data. This data is then translated into a huge matrix for better viewing and analysis. The use of radiomics and AI is particularly useful in nodule detection as well as the prediction of malignancy. When it comes to chest CT, AI integration has been focused on accurate nodule detection and the classification of benign and malignant tumors. However, an important factor that needs to be considered before nodule detection is the classification of lung nodules. They are categorized based on their texture and size into solid, part-solid, and non-solid. The incorporation of AI has enhanced the sensitivity of nodule sensing and reduced reading time, which has been a great advantage to radiologists and patients alike. While AI is extremely helpful in the diagnosis process, it is important to note that it should not be used as a first reader. Radiologists may miss the opportunity to analyze nodules missed by the computer. Therefore, AI has been approved as a second reader or is used in conjunction with the radiologist to provide the most accurate and efficient diagnosis possible.

Digital Pathology or Histopathology: Haematoxylin and Eosin (H&E) staining is a widely used method in diagnosing cancerous tissues. With the advent of technology, it has evolved into whole-slide imaging (WSI) of tissues, where virtual slides of the tissues are digitized so that CAD can be incorporated into the diagnosis process [46]. This digitization helps in the early recognition of tumors, leading to better disease prognosis. DL is another sub-class of ML that utilizes CNN to differentiate between different sub-types of lung cancer. These models essentially imitate biological neurons, thus helping in the advancement of diagnostic accuracy and the characterization of tumors. DL is especially helpful to pathologists, as it facilitates the detection of complicated patterns of tumors in enormous data sets [47]. For instance, in lung cancer diagnosis, Wang et al. constructed a CNN algorithm that helped dissect a tumor as either malignant or non-malignant, with an accuracy rate of approximately 89.8% [48]. Several applications of AI include recognition of cancer, prediction of prognosis, prediction of gene mutation, and detection of PD-L1 expression. The simple identification of cancer is termed image segmentation, which has other applications such as identifying the exact stage of cancer and the histological subtyping of lung cancer [49].

The diagnosis and treatment of cancer depend largely on the accurate detection of the TNM staging [50]. In addition to TNM staging, the classification of lung cancer into sub-types such as NSCLC and SCLC is also important as it assists pathologists in calculating the prevalence or ratio of the different sub-types in a particular specimen. This, in turn, can help predict gene mutation and guide treatment decisions. However, identifying the ratio of tumor cells is a complex and labor-intensive task that requires a high degree of accuracy. There is significant potential for errors, which can have serious consequences for patient care. To address this issue, an AI model was developed that can accurately measure the percentage of tumor cells in a specimen. The model was designed to work in conjunction with pathologists to minimize errors and provide a more accurate diagnosis. Together, the AI model and pathologists can ensure that cancer patients receive the best possible care by providing a proper, error-free conclusion [51]. However, there are certain limitations or demerits of AI that need to be overcome, such as misdiagnosis (underdiagnosis or overdiagnosis), high economic burden, and lack of privacy due to the disclosure of personal information.



## **Application of AI Tools in Prostate Cancer Detection**

The second most frequent type of cancer in men is called prostate cancer (PCa). In comparison to other cancers, it is linked to a high rate of morbidity and a low rate of fatality. It ranks as the sixth most common cause of death worldwide [52]. PCa diagnosis in the early stages is important as it leads to improved mortality or cancer-specific survival rate. Evaluation of **prostate-specific antigen** (**PSA**) levels or routine rectal examination are some of the screening tests for prostate cancer. Individuals with high PSA levels or an atypical rectal examination are advised for **Trans-Rectal Ultrasonography** (**TRUS**) [53]. In addition, **Multiparametric Magnetic Resonance Imaging** (mpMRI) is another beneficial tool used for the diagnosis of PCa. As prostate cancer is a diverse and complex disease with varying features and morphologies, it is difficult to diagnose early. Disease classification such as low-risk indolent cancer or high-risk aggressive cancer is very important, and this is often inaccurately analyzed or diagnosed. Therefore, the utilization of AI is necessary for early disease detection and proper risk stratification (figure 3).

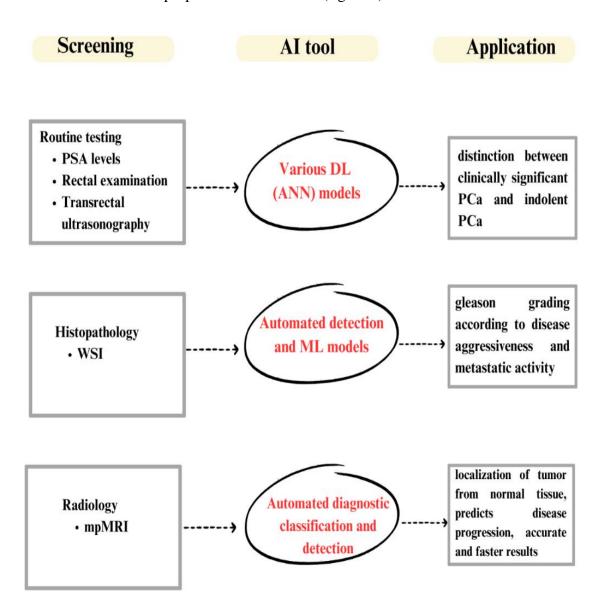


Figure 3. AI tools for Prostate cancer detection.



**Prostate Specific Antigens (PSA) Analysis:** PSA level analysis is one of the most customary tests performed for the detection of prostate cancer. Generally, a patient with a PSA level of more than 4 ng/ml is diagnosed with early-grade prostate cancer. Elevated PSA levels suggest prostate cancer, benign prostatic disease, prostatitis, or trauma, therefore accurate diagnosis is necessary for the prevention of false positive detections [53], [54]. In addition, PSA testing also includes the distinction between patients with clinically significant prostate cancer (csPCa) who should undergo a biopsy and patients with indolent prostate cancer who do not need to undergo a biopsy. Consequently, several AI algorithms are used for the proper detection of early-stage PCa and its progression. A study conducted by Djavan et al. described the diagnostic accuracy of PCa in patients by conventional statistical analysis of standard PSA guidelines, as compared to an ANN (DL) model. The sensitivity of the ANN model was 95% and it was concluded that the predictive accuracy of the AI model was higher than the conventional one [55].

Paige Prostate: It is an ML algorithm that is applied to whole slide images (WSI) to distinguish between benign and malignant tumors. The WSI acts as the input in the AI algorithm and the output or result is generated as either "suspicious" or "not suspicious" for PCa. It can be used in both ways as a first reader and as a second reader for accurate diagnosis of prostatic adenocarcinoma. For example, the algorithm can be run on the images and the "suspicious" lesions can be re-reviewed by expert pathologists to confirm the presence of malignancy. It can also be utilized as a second reader to identify any tumor cells or lesions missed by pathologists. The model assists oncologists in reducing diagnostic errors, improving efficiency, and concomitantly decreasing the workload of the pathologists [19]. Another model PathAI has developed a similar DL algorithm which is used in conjunction with pathology slides for accurate diagnosis of PCa. It is applied to H&E-stained WSIs to separate malignant tumors from indolent tumors. It also calculates a more accurate AI-based Gleason Score (GS) and the aggressiveness of the disease which results in a decrease in the false positive rates of PCa.

**Tempus:** It is a company that has developed several AI models for better cancer diagnosis. It improves the sensitivity and accuracy of the Gleason grading system thereby, preventing overdiagnosis or underdiagnosis leading to overtreatment or undertreatment, respectively. It focuses on providing a more accurate and targeted therapy for each patient, which in turn results in better disease prognosis [21]. Moreover, Prostate.ai offers several AI tools that are concomitantly used with imaging techniques such as MRI, TRUS, and even PET scans. The use of AI during MRI is very helpful as it significantly decreases the complexity of examining and understanding the mpMRI. It accurately detects suspicious lesions and performs segmentation of the prostate gland. It also calculates the PI-RADS score in two ways- a) utilizing an algorithm that gives out the PI-RADS score directly or b) using multiple algorithms with multiple outputs or results, which are then overlooked by expert pathologists to manually determine the final PI-RADS score [22], [56].

**Histopathology:** The introduction of AI is needed for proper grading and localization of the histopathological slides based on a Gleason score as per the International Society of Urological Pathology (ISUP) [54]. Gleason grading characterizes the disease according to its aggressiveness and metastatic ability. Low-risk, intermediate-risk, and high-risk are the three main categories, and the disease is further classified as per the Gleason grading. The low-risk group is associated with grade group 1 with a Gleason score (GS) of 3+3. Intermediate-risk groups consist of grade groups 2 and 3 where group 2 has GS 3+4, whereas group 3 has GS



4+3. Lastly, the high-risk groups contain grade groups 4 and 5 where group 4 has GS 4+4, 3+5, or 5+3, and group 5 has GS 4+5, 5+4, or 5+5 [22]. The overall Gleason score is calculated based on the different tumor patterns. The most common or dominant and the second most common types of patterns determine the net Gleason score. For instance, a small section of the slide may consist of high-grade cancer, and a large section may consist of low-grade cancer, then a combination of both is considered the Gleason score [57]. AI techniques such as automated detection have also been significantly used to classify histology slides. Various ML models are utilized to segment normal epithelial, stromal, and lumen cells from diseased cells. For example, Gertych et al. constructed various ML algorithms for the detection and segmentation of benign or normal epithelial and stromal components from malignant components [57], [58]. The role of AI in histopathology presents as a pre-processing stage before a more complex and detailed analysis of the specimen is done with radiologic imaging. The incorporation of AI in combined radiologic-pathologic techniques is also popular.

Radiology: mp MRI is a superior diagnostic tool used for the identification of PCa [59]. It utilizes T2-weighted imaging, diffusion-weighted imaging (DWI), and dynamic contrastenhanced sequences for better quality of the images leading to easier reading and analysis [57]. mp MRI is quite helpful for accurately detecting cancerous lesions, as well as identifying their degree of aggressiveness. The stratification or classification of suspicious lesions observed during mp MRI is done according to the Prostate Imaging Reporting and Detection System (PI-RADS). It is suggested in patients who have not undergone a biopsy but can also be done in patients who have undergone a biopsy. If PI-RADS score is less than or equal to 2, it is considered a low-risk PCa, and a biopsy may be unnecessary. On the other hand, if the PI-RADS score is more than or equal to 3, then the patient may have to undergo Trans-Rectal Ultrasonography Biopsy (TRUS-Bx) in combination with MRI-TBx [22]. However, compiling of numerous images in mp MRI and then examining them requires a certain technical skill set. Therefore, analysis and evaluation of all the sequences is challenging and the need for experts is highly required. Due to inter-reader variability, inaccurate detection of the lesions, and inability to predict metastasis of the tumor, the requirement of AI arises. Therefore, several AI algorithms, specifically ML models, have been employed to enhance or improve the diagnosis and detection of PCa. Automatic detection or automated diagnostic classification is widely used for accurate and faster results. Specifically, automatic detection is used for the recognition and localization of tumors, whereas automated diagnostic classification is used for the characterization of the lesions based on their aggressiveness. This is achieved by decreasing the inter-reader variability between urologists, as well as increasing the sensitivity of the detection of tumors [57]. Various algorithms can be used in conjunction or as a second reader with the radiologists for the detection of suspicious regions or lesions, and its consequent stratification [60]. For example, Wang et al. constructed a DL model for the detection of lesions, and this algorithm showed a sensitivity of 92%, but with one false positive lesion per patient [61]. Several algorithms perform tasks like classification of the identified lesions and prediction of tumor aggressiveness [62]. The implementation of AI with mpMRI increases its sensitivity and overall specificity of the detection of tumors.

## Application of AI tools in Colon Cancer Detection

It is a multifactorial malignancy that is associated with high mortality rates [63]. CRC is often identified in the advanced stages of the disease, thus impairing the prognosis and survival rate of a patient. However, early detection via routine screening has reduced cancer-related deaths



[64]. Colonoscopy, endocytoscopy, and computer tomography colonography (CTC) are frequently used to grade CRC. Although accurate, the results obtained are operator-dependent. Moreover, the difficulty in training endoscopists to effectively use these methodologies has led to variability in the adenoma detection rate (ADR). Thus, the application of AI in screening, detecting, and diagnosing CRC is warranted. The following AI tools are widely employed to accurately recognize and detect colon cancer. Such as:

Cosmo Pharmaceuticals - GI Genius<sup>TM</sup>: GI Genius<sup>TM</sup> is a CNN algorithm aimed at aiding endoscopists in the real-time detection of polyps and adenomas during white-light endoscopic examinations. Wallace et al. carried out a randomized cross-country controlled study wherein a subject pool of 230 patients was randomized to two consecutive colonoscopies, with and without AI, respectively. The adenoma miss rate (AMR) in the GI Genius arm was 15.5%, and the AMR in the control group was 32.4% (p < 0.001). The study concluded that the module was associated with a reduction in miss rates, thus emphasizing the benefit of AI in CRC screening (figure 4) [28]. **Iterative Health<sup>TM</sup> - SKOUT®:** Iterative Health developed SKOUT, an FDA-cleared polyp detection CADe module, to provide real-time judgment to endoscopists during colonoscopies. In a study, patients were randomly subjected to either standard or CADe-aided colonoscopies. The study aimed to determine the adenoma per colonoscopy (APC) value and true histology rate (THR). There was an increase in APC value with the CADe device (standard vs. CADe: 0.83 vs. 1.05, P = .002), while there was no decrease in THR values. It concluded that the CADe tool improved overall APC and ADR, with its utilization being beneficial in the early detection of malignancy (figure 4) [29].

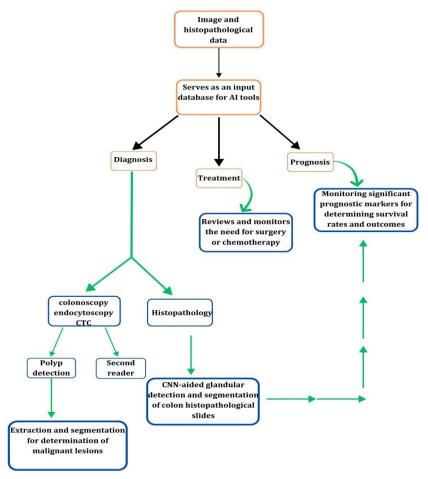


Fig. 4. AI techniques for colon rectal cancer diagnosis.



Colonoscopy: Early detection of preneoplastic lesions and colorectal polyps through colonoscopy is considered the "gold standard" for preventing colorectal cancer (CRC). However, this approach is hindered by factors such as the skill of the endoscopist and inadequate bowel preparation. Wang et al. investigated the impact of a DL-based CADe model on polyp and adenoma detection rates. Among 1058 patients, 536 underwent a conventional colonoscopy randomly, while 522 underwent colonoscopy aided by a CADe system. Implementing CADe is crucial to reduce polyp-miss rates and variability in adenoma detection rates. The results revealed that the AI model significantly increased both the adenoma detection rate (ADR) (29.1% vs. 20.3%, p<0.001) and the mean number of adenomas per patient (0.53 vs. 0.31, p<0.001), mainly due to detecting numerous diminutive polyps. Although no statistical difference was observed in the detection of large adenomas, there was an increase in the number of hyperplastic polyps in the CADe group (114 vs. 52, p < 0.001) [65]. In a prospective study by Mori et al., CADx combined with colonoscopy achieved a pathologic prediction rate of 98.1%, indicating real-time identification of neoplastic and non-neoplastic lesions, aiding in determining appropriate treatment strategies for diminutive polyps [66]. Becq et al. conducted a prospective single-center study involving 50 patients aged 50 years and older, with 31 being women, undergoing colonoscopy. Their procedural videos were analyzed using a DL algorithm to detect colorectal polyps, which were then reviewed by expert gastroenterologists. Overall, 55 polyps were removed by the endoscopist. The sensitivity of AI for polyp detection was 98.8%, with a polyp detection rate of 82% for the AI system compared to 62% for the endoscopist. This study demonstrated the effectiveness of the DL system in screening for malignancies even in cases of variable bowel preparation [67].

**Endocytoscopy:** This imaging modality utilizes a high magnification power of 520-fold, enabling real-time, in-vivo visualization at the cellular level, thereby facilitating "optical biopsy" or "virtual histology" of colorectal neoplasms [68]. Recent advancements in AI have further enhanced the capabilities of endocytoscopy. In a retrospective study, Takeda et al. evaluated the diagnostic accuracy of a CAD model for endocytoscopy (EC-CAD). They established an image database comprising 5843 endocytoscopy images of 375 lesions. From this dataset, 5543 images from 238 lesions were randomly selected to construct a diagnostic algorithm. This algorithm was then applied to the remaining 200 images. Of these, 188 were evaluated by the EC-CAD system. The sensitivity, specificity, accuracy, and negative and positive predictive values were 89.4%, 98.9%, 94.1%, 90.1%, and 98.8%, respectively [69].

Computer Tomography Colonography: CTC serves as a non-invasive imaging technique for staging CRC. Grosu et al. devised a machine learning (ML) methodology to distinguish between benign and premalignant colorectal polyps detected via CTC in average-risk, asymptomatic CRC patients. They achieved a sensitivity of 82%, specificity of 85%, and an AUC of 0.91, affirming its effectiveness as a non-invasive alternative for polyp categorization [70]. In a study by Ito et al., a convolutional neural network (CNN) was utilized in conjunction with endoscopy to diagnose cT1b CRC. The CNN exhibited high sensitivity and specificity for cT1b detection, suggesting the feasibility of quantitative diagnosis independent of operator skill and expertise [71].

**Histopathology:** Histopathology analysis is essential in the staging, risk stratification, and ultimately in the prognosis of CRC-afflicted patients. Sena et al. proposed a DL model capable of recognizing the four stages of cancer development. A database of 393 images was



created, which was used to validate and test the DL system. Overall, an accuracy of > 95% was achieved, although there was uncertainty in labeling due to overlapping in the four stages [72]. Alicja et al. proposed the use of ARA-CNN, which aimed to decrease the uncertainty in mislabeled images [73]. The analysis of glandular anatomy in colon histopathological images is an important prognostic factor for CRC. However, manual segmentation of the gland is labor-intensive and physician-dependent. Graham et al. developed a CNN for gland segmentation, achieving good performance [74]. Moreover, Shaban et al. proposed using CNN to classify histology images into normal, low-grade, and high-grade CRC [75]. Terradillos et al. developed a DL model trained with images obtained via multiphoton microscopy (MPM). They generated a dataset of 14,712 images, which was then used to train and validate the neural network. The AI had a sensitivity of  $0.8228 \pm 0.1575$  and a specificity of  $0.9114 \pm 0.0814$  for detecting cancerous lesions. The study concluded that the DL model could be used for in-situ diagnosis, thereby minimizing the need for invasive biopsies [76].

## **Application of AI tools in Cervical Cancer Detection**

Cervical cancer, an invasive epithelial tumor occurring within the cervix holds the 4th position in commonly diagnosed cancer in women, with the majority of cases resulting from recurrent HPV infections (particularly HPV types 16 or 18) [77], [78]. It is among the primary causes of mortality in developing countries, with an estimated global incidence of more than 600,000 new cases and associated 341,831 deaths, as reported in 2020 [79]. This cancer can be prevented and managed early using preventive strategies such as HPV vaccination and screening tests. Despite its implementation in clinical practice, the lack of skilled professionals [79], [80] and the inconsistency between pathology and colposcopy may lead to missed diagnosis and misdiagnosis, along with additional factors that have increased the global burden of this disease, requiring the search for novel strategies [81] (figure 5).

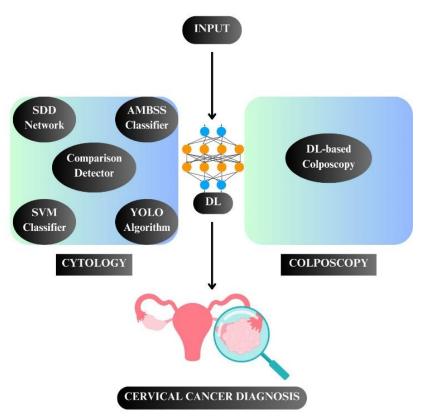


Fig. 5. AI techniques for cervical cancer diagnosis.



Cytology: In recent years, cervical cancer diagnosis has seen significant progress with the aid of DL techniques [82], [83]. Researchers have leveraged DL methods to classify cervical cells and develop computerized systems to assist medical professionals in diagnosis. In a study conducted by Jia et.al., cervical cells were classified using the Single Shot MultiBox Detector (SSD) network and a dataset of 1462 cervical cells. The results were promising, with an accuracy rate of 90.8% and a mean Average Precision (mAP) of 81.53% in classifying cervical cells [84]. This research offers a potential breakthrough in the detection and diagnosis of cervical cancer. Another study addressed the issue of data scarcity in DL-based techniques by proposing an optimal detection approach for cancerous cervical cells called a Comparison detector. The study reported that training on small datasets yielded an mAP of 26.3% and 35.7% of Average Recall (AR), while moderate-sized datasets resulted in mAP and AR of 48.8% and 64.0%, respectively [85]. Furthermore, Shiney and Rose developed three novel techniques for automated identification and categorization of cervical cancer in Pap smears, which can be a valuable tool for medical professionals in the diagnosis and treatment of cervical cancer. Overall, these studies highlight the potential of DL techniques in improving the accuracy and efficiency of cervical cancer diagnosis.

The use of Advance Map-Based Superpixel Segmentation (AMBSS) and Support Vector Machine (SVM) classifiers has enabled accurate classification of images with an 85.4% accuracy rate. However, to further enhance the accuracy of this process, two additional techniques were employed. The first technique involved the use of AMBSS with a quasinewton-based Feed Forward Neural Network classification, which reported an accuracy rate of 96.0%. The second technique involved the use of AMBSS with a Deep auto-encoder-based Extreme Learning Machine classification, which reported an impressive accuracy rate of 99.1% [30]. In another study, Jia et al. utilized the YOLO (You Only Look Once) algorithm for diagnosing cervical cancer. The results of this study showed a mean average precision (MAP) of 78.87%, which is higher than the MAP reported by SSD, YOLOv3, and ResNet50 by 8.02%, 8.22%, and 4.83%, respectively. These findings provide valuable guidance for future researchers in the field of developing a computerized cervical cancer diagnosis system [86].

Colposcopy: To diagnose high-grade CIN, Kim et al. employed computer-assisted colposcopy to evaluate its feasibility and reported enhanced sensitivity with almost equivalent selectivity of AI in detecting high-grade CIN compared with personal evaluations. In addition, they also found that when both assessments were combined (AI and two colposcopies), there was an increase in the accuracy rate in detecting lesions [87]. In another study, researchers using the DL-based colposcopy technique detected cervical precancerous lesions with 90.61% accuracy in distinguishing normal, low-grade squamous intraepithelial lesions (LSIL) from high-grade intraepithelial lesions (HSIL) and 91.18% accuracy in distinguishing LSIL, healthy controls, and HSIL [88]. Cho et al. developed and verified a DL system to obtain the automated classification of cervical neoplasms, and their results revealed 48.6% and 51.7% for the Inception-Resnet-v2 and Resnet-152 models, respectively, for the CIN system. The reported accuracies of the LAST system were 71.8% and 74.7% for the Inception-Resnet-v2 and Resnet-152 models, respectively. In addition, for the Resnet-152 models in the CIN and LAST systems, the AUC were 0.781 and 0.708, respectively [89].

#### MISCELLANEOUS CANCER

Blood cancer ranks lower in prevalence compared to other lethal cancers. It accounts for approximately 10% of diagnoses in the United States each year and has a mortality rate of 3%



in comparison to other cancers-associated mortality. There are various types of blood cancers such as Leukemias (Acute Lymphocytic Leukemia, Chronic Lymphocytic Leukemia), Lymphomas (Hodgkin's Lymphoma, B cell Lymphoma), and myelomas (Plasmacytoma). The most prevalent blood cancer in the United States is Leukemia which is quite common among children and adolescents. It is a type of cancer that does not have any classic or "hallmark" clinical features that would aid in its true diagnosis. The symptoms are indolent, and mild and can be seen in other types of diseases, therefore it is hard to detect. Therefore, the use of AI is helpful in the early diagnosis and differentiation of the malignancy. The most commonly used screening tool is peripheral blood smear (PBS) image analysis. Numerous AI methods have been employed on the PBS images for differentiation, counting of cancerous cells, and diagnosis. The ML algorithm essentially extracts features or components from the PBS images, and then the researchers analyze these features to help with the identification of any particular type of cancer. Some feature types include texture features, color features, and morphological features. On the other hand, the DL algorithms extract components of the images and evaluate and classify them with several CNN algorithms [90], [91]. Unlike the ML approach, DL models do not require any researchers for the classification of the extracted features. Another important step is segmentation which typically takes place before the feature extraction process. It is a pre-processing step and helps in better analysis of the extracted components. An example of segmentation is the removal of a blood cell or its nuclei from other blood cells, and this segmentation will help in predicting the accurate type of cancer and its sub-types. Multiple ML algorithms are used to perform segmentation to differentiate or separate the boundary from the nucleus and cytoplasm to achieve better characterization of the cancer [90], [92]. Therefore, the role of AI is essential in the PBS images as manual examination of the images is quite time-consuming and tedious. Furthermore, there is more margin for error in the manual process, as various factors vary from person to person such as staining time, film thickness, blood thickness, etc.). Use of ML and DL is essential in PBS images for the diagnosis of leukemia and other blood-related diseases as well.

DermaSensor Inc. - DermaSensor TM: It is a highly reliable adjunctive diagnostic tool cleared by the FDA for clinicians to use on skin lesions indicative of skin cancer. The device utilizes a combination of AI and elastic scattering spectroscopy (ESS) to extract information regarding histopathological changes[93]. It is important to note that DermaSensor<sup>TM</sup> is designed to serve as a second reader and is not a stand-alone diagnostic aid. Hartman et al., through a large-scale prospective, investigator-blinded, multicenter study, scrutinized the capability of the ESS tool in the detection of melanomas. A subject pool of 311 patients was involved, all of whom presented with skin lesions clinically consistent with melanomas, and were examined using DermaSensor<sup>TM</sup>, followed by a biopsy for histopathological evaluation. The results were impressive, with a sensitivity of 95.5% (95% CI, 84.5% to 98.8%, 42 of 44 melanomas) and a specificity of 32.5% (95% CI, 27.2% to 38.3%) for malignant melanoma detection. Therefore, based on the study's conclusion, DermaSensor<sup>TM</sup> is a highly useful aid for melanoma detection [94].

DL has emerged as a highly promising tool for various applications in gliomas, including segmentation, classification, and genomic marker prediction, with proven success rates [95], [96]. The technology, coupled with MRI images, has demonstrated an impressive accuracy of 99% in diagnosing pituitary tumors and meningiomas [97]. Moreover, the utilization of PET and MRI has been evaluated in predicting disease progression in aggressive gliomas [98]. With the latest advancements, these technologies can now be employed in pediatric brain



tumors, such as pilocytic astrocytoma, brainstem glioma, medulloblastoma, and ependymoma, hinting at an imminent future in the diagnostic workup for different forms of brain tumors [99].

#### LIMITATIONS AND CHALLENGES OF AI IN DIAGNOSIS

Although AI has its advantages, it has several drawbacks that can impede its clinical use, necessitating further investigation. These techniques necessitate a wealth of information to learn and provide precise, dependable, and comprehensive forecasts that include the actual patient population. The data quality of AI must be excellent, with a variety of diversity to reflect real-world practice. Poor quality data can result in incorrect or missed diagnoses, affecting generalizability [100], [101]. AI can indeed make accurate cancer diagnoses, but a major limitation is the black-box nature of its reasoning, rendering it non-understandable [101]. It is important to note that while AI is a valuable technology, it can never fully replace the expertise and practical knowledge of well-trained medical professionals such as pathologists and radiologists. These professionals possess an in-depth understanding of the complexities involved in diagnosing cancer. AI can, however, serve as a complementary tool to aid clinicians in making more precise predictions and diagnoses of cancer [102].

The implementation of this technology in real-world practice is fraught with a variety of challenges that cannot be overlooked. Regulatory and ethical considerations, integration with established healthcare systems such as medical imaging systems and electronic health records (EHRs), and the burden on clinicians cannot be ignored. The generated predictions by AI require review, verification, and validation by medical professionals, which necessitates resources and expertise to confirm the accuracy and dependability of these outputs [103].

#### **CONCLUSION**

In conclusion, the integration of artificial intelligence, particularly machine learning, into the realm of cancer diagnosis and prognosis marks a groundbreaking advancement in healthcare. The relentless battle against cancer, with its rapid progression and high mortality rates, has found a formidable ally in AI technology. The ability of AI algorithms and predictive models to analyze vast datasets with unparalleled accuracy has transformed our understanding of the disease, offering unprecedented insights into its complexities. The strides made in early detection through AI-driven technologies have not only enhanced patient survival rates but have also ushered in a new era of personalized and targeted therapies. The precision and efficiency with which AI aids medical professionals in navigating the intricate landscape of cancer research cannot be overstated. It has not only accelerated the pace of discovery but has also opened avenues for innovative approaches to treatment and management. However, this transformative journey is not without its challenges. Practical considerations, ethical concerns, and the need for seamless integration into healthcare settings pose significant hurdles. Striking a delicate balance between the immense potential of AI and its responsible and ethical implementation is crucial.

In essence, the significance of AI in cancer healthcare is undeniable, with its benefits far outweighing the drawbacks. This comprehensive analysis has shed light on the game-changing impact of AI in the fight against cancer, emphasizing its role in early detection, prognosis, and personalized treatment strategies. As we navigate the evolving landscape of healthcare, embracing the potential of AI while addressing its challenges will undoubtedly pave the way for a future where the devastating impact of cancer is mitigated and therapeutic outcomes are optimized for the benefit of patients worldwide.



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The authors affirm that they have no known financial or interpersonal conflicts that would have seemed to have an impact on the research presented in this study.

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