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Artificial-Intelligence-Driven Precision Medicine in Cancer Treatment

Maya Hassane

ABSTRACT

Cancer continues to be a global health challenge, with millions of new cases and deaths each year. Recent advances in artificial intelligence (AI) are revolutionizing cancer care by enhancing precision medicine approaches. This review focuses on AI's applications in the detection, diagnosis, and treatment planning of the four most prevalent cancers in both genders. AI-driven tools have enhanced the precision of breast cancer diagnosis, reduced false positives in prostate cancer screening by up to 50%, and enhanced non-invasive diagnosis of both lung and colorectal cancers. AI models have demonstrated significant improvements in most aspects of cancer management, including reduction of treatment delays and improvement of clinical outcomes, making them critical for individualized treatment strategies.

Keywords: Artificial intelligence, Cancer treatment, Deep learning, Machine learning, Precision medicine

Introduction

Cancer remains one of the leading causes of morbidity and mortality worldwide. In 2022, cancer was responsible for 20 million new cases and 9.7 million deaths globally. Lung cancer was the most commonly diagnosed cancer, accounting for approximately 12.4% of all cases and 18.7% of cancer-related deaths. This was followed closely by breast, colorectal, and prostate cancers, which represented 11.6%, 9.6%, and 7.3% of new cancer cases, respectively¹ (Figure 1). These numbers underscore the ongoing burden of these major cancer types on global health and highlight the importance of continued efforts in cancer detection, diagnosis, and treatment improvement. Cancer treatment might be affected by genetic-, immune-, and lifestyle-related factors that are specific to each person. For this reason, precision medicine (PM), which tailors treatments to the individual characteristics of each patient, has become a critical approach in oncology.²

The advances in artificial intelligence (AI), machine learning (ML), and deep learning (DL) have brought a new dimension to PM, offering tools that can analyze vast datasets, identify patterns, and make predictions that enhance cancer treatment outcomes. AI refers to a field of computer science that focuses on creating systems capable of performing tasks that typically require human intelligence.³ ML is a subset of AI that involves the development of algorithms enabling computers to perform specific tasks by learning from large datasets without being programmed, thus identifying patterns and making decisions.³ DL is a subset of ML that involves the use of neural networks with multiple layers to understand complex data, allowing the machine to learn and make intelligent decisions⁴ (Figure 2). AI,

ML, and DL have demonstrated significant potential in understanding tumor biology, improving the accuracy of cancer diagnosis, assisting in risk stratification, predicting disease outcomes, and tailoring treatment plans to individual patient profile.^{5,6}

Early detection represents the first step towards better cancer management and patients' care improvement. A better understanding of cancer evolution, along with the development of highly sensitive detection technologies, is necessary to adapt proactive screening strategies, even before symptoms appear. These approaches involve using biomarkers, imaging, genomics, proteomics, and AI to detect cancer-specific signals.^{7,8} AI and radiomics have revolutionized oncologic imaging by enhancing cancer detection and characterization, and monitoring response to treatment. Focusing on the three most common types of cancer (lung, breast, and colorectal), AI-driven techniques were shown to be effective in processing vast amounts of data generated by imaging modalities.⁹ FDA-approved AI tools have been integrated into the clinical practice in oncology, thereby participating in the improvement of cancer management. AI devices are mainly used in the diagnostic areas, particularly radiology and pathology, where they account for more than 80% of the approved devices. The year 2021 witnessed the largest number of AI devices that were used in the diagnosis of breast cancer (31%), followed by lung and prostate cancers (8.5% each) and colorectal cancer (CRC) (7%).¹⁰ Through ameliorating cancer detection, diagnosis, and prognosis, AI can improve patients' treatment planning and can shift cancer therapy from a "one-size-fits-all" approach into a more tailored and individualized strategy.^{8,11}

The current study examines the applications of AI in oncology, with a particular focus on the three most prevalent cancer types affecting males and females. In this mini-review, we assessed the contribution of AI into PM, through the different phases of cancer management (Figure 3). We provided a summary of the role of AI, including ML and DL, in enhancing cancer detection, diagnosis, and treatment planning, and we mentioned some of the challenges that AI is facing in the oncology landscape.

AI Application in Breast Cancer

Breast cancer is the leading cause of cancer deaths and the most commonly diagnosed cancer in females, with 2.3 million new cases being estimated in 2022.¹ AI, particularly DL models, has advanced the detection, prognosis, and treatment of breast cancer with notable improvements in reducing false positives and processing complex multi-omics, genomic, and radiomic data. DL models have achieved an accuracy of up to 98.58%

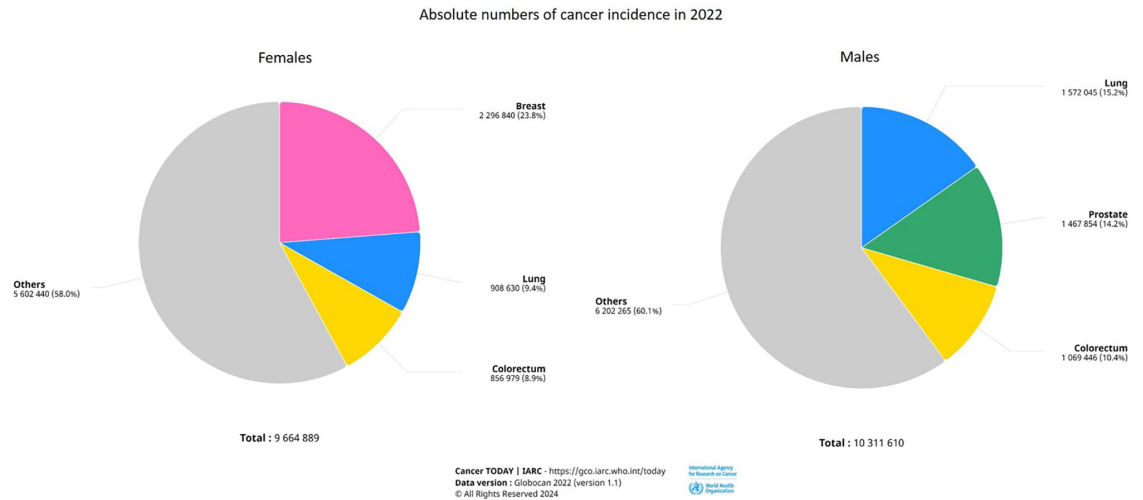


Fig 1 | Absolute numbers of cancer incidence in 2022, both in males and females

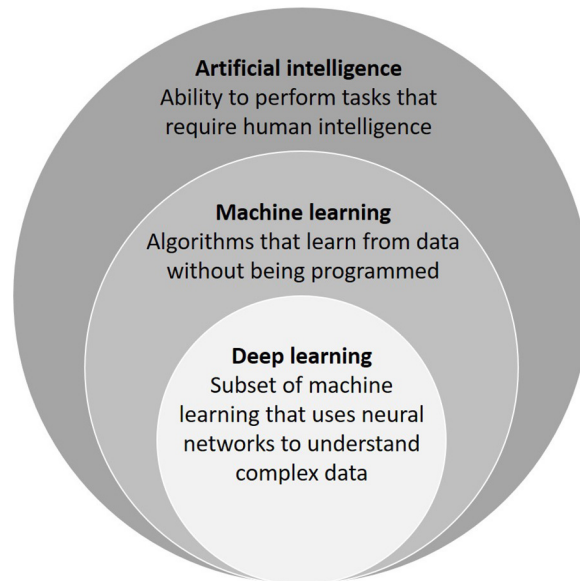


Fig 2 | Overview of AI, ML, and DL

in diagnosing breast cancer and have shown great potential in reducing unnecessary treatments, enhancing precision oncology, and improving clinical outcomes in breast cancer management.¹²⁻¹⁴

Mammography is the primary line of screening for breast cancer, but interpretation of its images remains challenging, leading to possible false positives and false negatives. While false positives can result in unnecessary procedures and patients' concerns, false negatives can delay cancer detection until it reaches a less treatable stage. Using an AI system to predict breast cancer through mammogram interpretation across large datasets from the USA and the UK, a significant reduction in both false positives (5.7% in the USA and 1.2% in the UK) and false negatives (9.4% in the USA and 2.7% in the UK) was observed. The AI system exhibited a better performance compared to human radiologists in analyzing mammogram results

to predict breast cancer.¹⁵ DL models have also made significant advances in breast magnetic resonance imaging (MRI), where they have demonstrated high accuracy in diagnosing breast cancer, classifying molecular and histopathological types, and detecting lymph node metastasis (LNM).¹⁶ Accurate prediction of lymph node involvement in breast cancer can guide surgeons in identifying the stage of the disease and making informed decisions about the extent of surgery required, potentially sparing patients from unnecessary, time-consuming, costly, or invasive procedures. The TabNet DL model can predict metastasis in sentinel lymph nodes, the first lymphatic nodes that receive metastatic deposits of cancerous cells, in breast cancer patients in an accurate, specific, and sensitive way, based on pre-operative clinicopathological features.¹⁷ In the same context, axillary lymph node metastasis can be predicted by DL

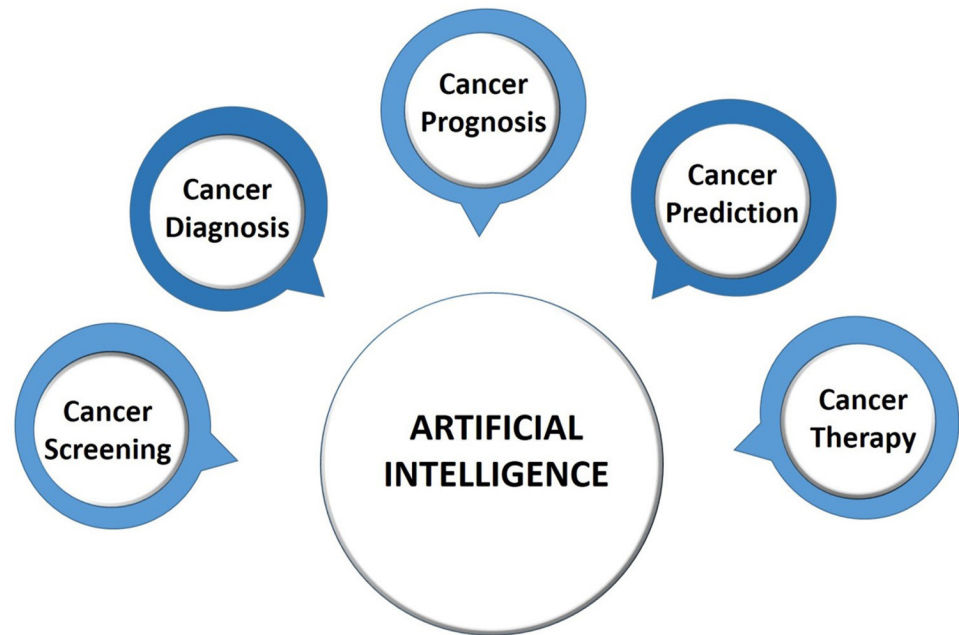


Fig 3 | AI applications in oncology

models in breast cancer patients using pre-processed computed tomography (CT) images together with clinical insights. The model could also detect subtle changes in lymph node margins and adjacent soft tissues, which are often difficult for human experts to identify.¹⁸

To assess the tumor aggressiveness in breast cancer, the Nottingham Histological Grading (NHG) is applied to classify tumors into grades, with the lower grade being associated with better prognosis and better-predicted treatment outcome. The predGrade DL model, which was trained and tested on histological whole-slide images (WSIs), was designed to replicate the NHG system. The predGrade model was able to stratify patients into three risk groups and accurately predict recurrence-free survival, while reducing the variability and subjectivity associated with manual NHG assessments.¹⁹

Neoadjuvant treatment, defined as chemotherapy associated or not with targeted therapy, administered before surgery, is increasingly used in the management of breast cancer to improve rates of breast-conserving surgery and increase patients' survival. Through combining clinical, digital pathology, genomic, and transcriptomic data from pre-treatment biopsies of breast tumors, an ML model has been developed and validated to predict the response of breast cancer patients to neoadjuvant therapy. The ML model has integrated multi-omic features such as tumor proliferation, immune activation, and genetic mutations and has demonstrated high accuracy in predicting pathological complete response to neoadjuvant treatment.²⁰ DL models have also shown potential in guiding adjuvant chemotherapy decisions for elderly breast cancer patients, a group for whom chemotherapy benefits are often debated due to

age-related risks, and surgical excision is often considered the treatment of choice. The BITES DL model was able to provide individualized chemotherapy recommendations associated with a 12% reduction in mortality and an eight-month extension in survival over ten years.²¹

Kinase inhibitors, through interrupting the cell-cycle activation necessary for cancer proliferation, represent an important target in drug development for cancer treatment. Despite benefiting from improved outcomes following treatment with kinase inhibitors, metastatic breast cancer patients often develop resistance to this class of drugs with time. Integrating genetic alterations across multiple protein assemblies, a DL model was developed to predict breast cancer response and resistance to kinase inhibitors, particularly palbociclib. The model outperformed traditional single-gene biomarkers and was efficient in patient-derived xenografts and clinical applications.²²

AI Application in Prostate Cancer

Prostate cancer is the second most common type of cancer in males after lung cancer, with an estimated 1.5 million new cases being diagnosed in 2022.¹ Biopsy evaluation remains one of the most decisive techniques for diagnosing prostate cancer.²³ AI, particularly through ML and DL, has demonstrated a transformative potential in prostate cancer care. It has significantly improved early diagnosis, risk stratification, and treatment decision-making in both localized and advanced prostate cancers. In localized prostate cancer, progress has been made in different stages of the disease, including improved and early detection, diagnosis, targeted biopsy, grading, segmentation, disease prognosis, and outcome prediction. In metastatic prostate cancer, AI has facilitated the quantification of

metastatic burden, the accurate identification of castration resistance, and the prediction of treatment sensitivity and resistance. Integrating multimodal data, including imaging, genomics, and clinical information, holds promise for refined prognosis and personalized treatment selection.^{24,25}

Prostate volume (PV), in combination with prostate-specific antigen (PSA), yields PSA density, an important biomarker to identify the risk of prostate cancer. Using MRI, a DL algorithm outperformed radiologists in assessing PV, with lower bias and better precision and agreement with reference standards.²⁶ Through improving MRI image quality, AI has ameliorated prostate segmentation, cancer-suspicious region detection, and prostate lesion classification, which are crucial for accurate and early diagnosis.²⁷ Prostate segmentation is a routine evaluation in which prostate MRI is analyzed slice-by-slice by a clinician. Besides being time-consuming, prostate segmentation requires a well-trained radiologist and is subject to intra- and inter-observer variability. DL models, trained on clinically generated prostate segmentations from MRI scans, have shown potential in significantly enhancing prostate cancer diagnosis through DL-based segmentation.^{28,29} The accuracy of prostate cancer diagnosis can also be improved by reducing the interference caused by rectal artifacts. Using MRI, a DL model was designed to achieve this goal by reducing false-positive and false-negative detections caused by these artifacts.³⁰

The Gleason grading method is the primary prognostic indicator for locally confined prostate cancer and a critical predictor of prostate cancer recurrence; it gives a lower score for the tissue from a biopsy that resembles healthy tissues, and a higher score for abnormal tissues.³¹ However, this manual grading system is time-consuming and is subject to significant inter-observer variability; these issues were addressed by the development of DL algorithms that achieved a performance similar to pathologists and demonstrated excellent accuracy for histopathologic diagnosis and Gleason grading of prostate cancer, using biopsy specimens.^{32,33} In the same context, an AI system, trained on over 10,000 MRI scans and evaluated against the performance of 62 radiologists from several centers worldwide, has achieved superior accuracy compared to the radiologists in identifying Gleason grade group 2 or higher cancers. The AI system detected 6.8% more clinically significant cancers at the same specificity as radiologists and significantly reduced false positives by 50.4%.³⁴

AI-biopsy is an advanced DL model that integrates MRI and histopathology data to enhance the diagnostic classification of prostate cancer, traditionally performed by the PI-RADS (Prostate Imaging Reporting and Data System) scoring system. The AI-biopsy fully automated model demonstrated higher agreement with biopsy results compared to PI-RADS and outperformed the traditional scoring system in classifying cancer versus benign cases and differentiating high-risk from low-risk tumors.³⁵ Combining a DL model that uses biparametric MRI (bpMRI) with PI-RADS

significantly improved the specificity of clinically significant prostate cancer (csPCa) detection, thereby reducing unnecessary biopsies and enhancing the precision of csPCa diagnosis.³⁶ Adverse pathology (AP) in prostate cancer is a predictor for distant metastasis and is often associated with aggressive prostate cancer outcome. AP detection is critical for selecting appropriate therapeutic interventions. TransNet is a DL model designed to detect AP in prostate cancer using bpMRI. When integrated with clinical characteristics, TransNet outperformed traditional clinical models and radiologist interpretations in detecting AP.³⁷

DL has been implicated in enhancing the prediction of prostate cancer treatment outcomes. P-NET, a biologically informed DL, can predict advanced prostate cancer and potential recurrence by analyzing patients' genomic profiles. This model succeeded in stratifying prostate cancer patients based on their resistance to treatment and in assessing the molecular drivers behind this resistance. P-NET was designed in a way that allows researchers to view the multiple biological pathways involved in prostate cancer, thus providing them the tools to analyze these pathways and translate their findings into therapeutic approaches.³⁸

AI Application in Lung Cancer

Lung cancer is the leading cause of cancer death worldwide, being responsible for almost 1.8 million deaths in 2022.¹ AI technologies, including ML and DL, are extensively studied in the field of lung cancer, with 2,931 research articles being published about AI and lung cancer between 2003 and 2023.³⁹ AI-driven tools have been increasingly integrated into the management of lung cancer; they have improved early lung cancer detection, classification, and outcome prediction, through handling vast amounts of data generated from imaging, pathology, and clinical records.^{40,41} AI algorithms could predict lung cancer stage, lymph node involvement, distant metastases, tumor recurrence after surgery, and prognosis after therapy, thus helping clinicians in the decision-making process.⁴²

CT scan is the most commonly used method for lung cancer diagnosis. However, differentiating between the two main types of lung cancer—small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC)—can be challenging using the CT scan. SCLC and NSCLC differ significantly in terms of treatment approaches and survival outcomes. An ML-based classifier developed from radiomic features extracted from CT scans was successful in differentiating between lung cancer subtypes, promoting a non-invasive method for early lung cancer diagnosis.⁴³ Using contrast-enhanced CT images, DL-based radiomics models can also accurately predict LNM, an essential factor in classifying the severity of lung adenocarcinoma (LUAD).⁴⁴ DL models have shown potential to assist pathologists in accurately classifying the lung cancer subtype and predicting mutations from histopathology WSIs, which can significantly affect the diagnosis and treatment plan for the patients.⁴⁵

Liquid biopsy is an emerging technology in cancer diagnosis; it is a non-invasive alternative to surgical biopsies that can detect tumor-specific markers in body fluids. Circulating tumor DNA (ctDNA) is a key biomarker of liquid biopsy, whose detection after curative therapy indicates the presence of residual tumor cells. A novel bioinformatic tool, ECLIPSE, revealed an association between post-operative ctDNA detection and both NSCLC relapse and metastatic dissemination, following analysis of ctDNA clonal composition at low levels. Pre-operative absence of ctDNA distinguished biologically slow-growing LUAD with favorable outcomes. Furthermore, pre-operative analysis showed that subclones leading to future metastasis were more expanded than non-metastatic ones, offering new insights for neoadjuvant trials and understanding metastatic progression via liquid biopsy.⁴⁶

Immune checkpoint inhibitors (ICIs) are a class of drugs that block checkpoint proteins, molecules found on immune cells that help tumors evade the immune system. ICIs, such as the FDA-approved programmed death ligand 1 (PD-L1) blockers, enable the immune system to recognize and attack cancer cells.⁴⁷ AI-driven analyses of standard-of-care images, particularly through DL and radiomics, can enhance the precision of treatment by predicting patient responses to immunotherapy. These technologies can overcome the challenges of personalized treatment by considering the tumor heterogeneity, tumor microenvironment (TME), and treatment resistance mechanisms, which are all critical in determining the success of immunotherapy in lung cancer patients.⁴⁸ Using single-cell RNA sequencing data, a sophisticated AI network, integrating ML and DL algorithms, succeeded in identifying genes associated with LUAD epithelial cell stemness, which were used to construct a stemness-related gene signature (SRS). The SRS effectively stratified patients into high- and low-risk groups, with the high-risk group showing reduced immune cell infiltration and poorer response to immunotherapy. Experimental validation revealed that the top SRS gene, *CKS1B*, plays a crucial role in LUAD cell proliferation, migration, and invasion, suggesting its potential as a therapeutic target.⁴⁹ Moreover, through an AI-assisted platform that integrates multi-omics data with clinical information, an ongoing study (I3LUNG) is assessing patients diagnosed with advanced NSCLC (aNSCLC) and treated with immunotherapy. Despite the success of immunotherapy in treating aNSCLC, only a fraction of patients experience long-term benefits. By developing an AI-based decision support system that can accurately predict responses to immunotherapy, the limitations of current biomarkers could be successfully overcome. By providing individualized treatment recommendations, the I3LUNG study hopes to improve patient outcomes, reduce unnecessary toxicity, and optimize healthcare resources.⁵⁰

AI Application in CRC

CRC is the third cause of new cancer cases and cancer deaths in both males and females worldwide.¹ AI has

shown potential in improving the detection, diagnosis, and treatment of CRC by enhancing the accuracy and efficiency of existing methods. AI models are employed to detect and characterize CRC during endoscopic and laparoscopic procedures, predict personalized treatment options, and improve drug discovery processes.⁵¹⁻⁵⁴

Serum extracellular vesicles (EVs) are small particles that carry molecular cargo; they participate in intercellular communication and represent important biomarkers in liquid biopsy. Through analyzing proteomic profiles of serum EVs, ML models can outperform traditional biomarkers in diagnosing CRC at an early stage and successfully distinguishing between CRC and benign colorectal diseases.⁵⁵ DL models have also shown potential in diagnosing CRC subtypes using histopathological images⁵⁶ and distinguishing between malignant and benign colorectal lesions using colonoscopy images.⁵⁷

The TME is a structured ecosystem surrounding a tumor in which cancer cells interact with various non-cancerous components, including immune cells. TME plays a crucial role in cancer development, progression, and response to therapies, making it a potential therapeutic target in cancer treatment.⁵⁸ The subtype, density, and location of cells in the TME predict the clinical outcome of CRC. A multi-stain DL model (MSDLM), AImmunoscore, can predict prognosis and therapy response in CRC patients by analyzing the TME. Trained on immunohistochemistry (IHC) images from CRC patients, MSDLM outperformed the single-stain models in predicting relapse-free survival (RFS), and the existing clinical, molecular, and immune-based parameters in prognosticating CRC.⁵⁹

Mismatch repair deficiency (dMMR) leads to microsatellite instability (MSI), a characteristic pattern of DNA damage that correlates with a favorable response to ICIs in advanced disease and a poorer response to adjuvant chemotherapy in stage II CRC patients. dMMR and MSI are universally tested by multiplex polymerase chain reaction or multiplex IHC panel, but due to the high cost of both techniques, dMMR and MSI are not tested in all CRC patients. A DL system was designed to detect dMMR and MSI in CRC using routine hematoxylin and eosin (H&E)-stained slides, thus minimizing the cost and guiding the patients towards the right treatment plan, whether it is adjuvant chemotherapy or immunotherapy.⁶⁰ The efficacy of immunotherapy in cancer patients is often observed in patients with high values of tumor mutational burden (TMB), which is the total number of coding mutations in a tumor. Several techniques exist to determine TMB, such as whole genome, whole exome, or targeted gene panel sequencing. However, these methods are expensive and time-consuming. AI has been applied to offer a cheaper and faster alternative to traditional TMB evaluation methods, through clinical data and histopathological analysis of H&E-stained slides only.⁶¹

Recurrence after curative resection is the most common cause of death in patients with non-metastatic CRC. Using WSIs, a DL-based recurrence

risk score (DL-RRS) was developed to stratify patients with non-metastatic CRC into low- and high-risk groups. The DL-RRS demonstrated strong predictive performance, where high DL-RRS benefited more from adjuvant chemotherapy and had significantly worse RFS compared to those with low DL-RRS.⁶² Disease-free survival and overall survival (OS) are traditionally predicted by the TNM staging, a standard method for classifying the extent of cancer spread. A DL signature, developed based on WSIs stained with H&E, was shown to be an independent prognostic factor that outperforms TNM staging in patients' risk stratification.⁶³

Though surgery is the treatment of choice in CRC patients, its complexity has limited the integration of AI into this procedure. AI has been included in simple intraoperative steps, mainly related to computer vision. The da Vinci System is a robotic surgical technology used to assist in minimally invasive surgery like laparoscopy. It is beneficial in minimizing scarring, incisions, and pain, as well as reducing the time of hospitalization, period of recovery, and loss of blood. However, autonomous robotic surgeries are still part of the future and represent several challenges to be addressed.⁶⁴

AI in Cancer Treatment Response Prediction

An accurate prediction of the response to cancer therapy is beneficial for both the patients and the healthcare system. It will improve treatment effectiveness, minimize side effects and relapses, and reduce costs and use of resources. ENLIGHT-DeepPT is a DL framework that predicts cancer treatment responses by integrating histopathology images with transcriptomics. The DL model operates in two stages: DeepPT predicts gene expression profiles from routine H&E-stained tumor slides, and ENLIGHT uses DeepPT results to predict patient responses to targeted and immune therapies. The model was validated across multiple cancer types, including breast and lung cancers, and demonstrated that it can accurately predict responders without requiring direct training on treatment datasets.⁶⁵

ML models can predict the effectiveness and potential toxicities of ICIs in cancer treatment using real-world electronic health record (EHR) data, which will not require additional data collection from the patients. The risks of pneumonitis, colitis, hepatitis, and OS one year after ICI initiation were predicted in over 2,200 patients treated with ICIs.⁶⁶ LORIS, a logistic regression-based immunotherapy-response score, can also predict patient outcomes with immune checkpoint blockade (ICB) therapy across 18 solid tumor types, including colorectal, breast, and lung cancers. Using a dataset of 2,881 ICB-treated patients, the study demonstrates that LORIS outperforms existing biomarkers, such as TMB and PD-L1 expression, the two major FDA-approved biomarkers for ICB therapy, in predicting ICB response and survival. LORIS uses six readily measurable features (age, cancer type, TMB, systemic therapy history, blood albumin level, and blood neutrophil-to-lymphocyte ratio), providing

a transparent and interpretable method for patient stratification.⁶⁷

Current Challenges and Future Perspectives

Despite the increasing progress of AI in improving PM in cancer treatment, several challenges still need to be addressed. One major ethical concern is respecting patients' privacy, and maintaining the integrity of the doctor-patient relationship. The use of personal medical information or EHRs to train AI models should be prohibited without patients' consent. Misuse of such sensitive personal data can lead to loss of confidence in AI tools and breaches the right of patients to have confidential health records that are only shared privately with their doctor. Besides this ethical issue, many technical and regulatory concerns might also limit the implementation of AI into the healthcare system.^{68,69}

The "black box" concept of AI algorithms makes them hard to interpret by clinicians, who need to understand the reasoning behind AI-driven decisions to trust and effectively use these tools.^{68,69} However, improvements in explainable AI, which can provide insights about how and why AI reached a specific result or decision, might be able to solve the "black box" problem in the future.⁷⁰

AI models require large, high-quality datasets for training, but limited or incomplete data in cancer research limits the model development and its clinical applications. However, relaxing common eligibility criteria can safely increase the pool of eligible patients, thus enhancing trial inclusivity without negatively affecting the outcome.⁶ In addition, DL models are now able to solve the problem of missing data in cancer survival analysis; instead of discarding the incomplete data, which could affect the prediction outcome, DL models can ignore the missing values and predict the survival of lung cancer patients.⁷¹

AI integration into the healthcare system requires standardized and actionable guidelines to improve data diversity and transparency and to address the risks of algorithmic bias and health inequities.⁷² Given that AI models are trained on non-representative data, algorithmic bias might result in inaccurate predictions for underserved populations, who may have limited access to cutting-edge technology. This can lead to impaired prediction outcomes and can promote diagnosis and treatment inequality between minorities and the rest of the population. These disparities need to be addressed through specific guidelines that are created to ensure equal access to AI-enhanced treatments across the population. All patients must benefit from the advancements in PM to avoid any health disparities. To resolve this issue, the STANDING Together initiative seeks to establish consensus-based standards for ethical and equitable AI applications, with a proper inclusion of diverse populations and demographic groups.⁷²

AI-driven PM is transforming cancer treatment by enabling personalized approaches that target the unique characteristics of each patient's disease. While

significant progress has been made in applying AI to cancer detection, diagnosis, and treatment planning, there are still ethical and regulatory challenges to be addressed. Future research should focus on addressing these challenges and on improving the implementation of AI in the different aspects of cancer management. By continuing to innovate and collaborate across disciplines, the full potential of AI-driven PM in cancer treatment can be unlocked, ultimately improving patient outcomes and reducing the burden of cancer worldwide.

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