

International Journal of Multidisciplinary Research in Biotechnology, Pharmacy, Dental and Medical Sciences (IJMRBPDMS)

Explainable Artificial Intelligence for Predicting Cancer Treatment Toxicity in Real-World Clinical Practice

Dr. Jayanthi Kanaka Ram¹

¹Consultant ENT, elova hospitals, Bengaluru, india
jayanthikr33@gmail.com

ABSTRACT

Background:

Cancer treatment-related toxicities remain a major challenge in oncology, frequently compromising patient quality of life, treatment adherence, therapeutic efficacy, and overall survival. The increasing availability of real-world clinical data (RWD), combined with advances in artificial intelligence (AI) and machine learning (ML), has created new opportunities for the early prediction of treatment-related adverse events and personalized toxicity risk assessment.

This review provides a comprehensive overview of AI-driven approaches for predicting cancer treatment toxicity using real-world clinical data. It examines the application of conventional machine learning, deep learning, and emerging foundation models across diverse data sources, including electronic health records, genomic and molecular datasets, medical imaging, laboratory parameters, wearable device data, and patient-reported outcomes.

Machine learning models have demonstrated encouraging predictive performance for identifying treatment-related adverse events. Among the commonly used algorithms, random forest has been the most frequently applied, followed by support vector machines, XGBoost, decision trees, and LightGBM. A recent meta-analysis reported a pooled sensitivity of 0.65, specificity of 0.89, and an area under the receiver operating characteristic curve (AUC) of 0.8069, highlighting the potential of AI-based models for clinical toxicity prediction. Recent advances in transformer-based architectures, multimodal learning, and large language models have further improved predictive accuracy and model generalizability across multiple cancer types, treatment modalities, and healthcare settings. Foundation models trained on large-scale multimodal real-world datasets are emerging as promising clinical decision-support tools capable of integrating heterogeneous patient information for individualized toxicity prediction.

AI-driven toxicity prediction has the potential to transform precision oncology by enabling proactive patient monitoring, individualized treatment planning, dose optimization, early intervention, reduced treatment-related hospitalizations, and improved clinical outcomes. Despite these advances, challenges related to data quality, model interpretability, external validation, fairness, and seamless clinical implementation remain significant barriers to widespread adoption. This review summarizes current evidence, discusses emerging technologies, identifies existing limitations, and highlights future directions for integrating AI-driven toxicity prediction into routine oncology practice.

Keywords: Artificial intelligence; machine learning; deep learning; cancer treatment toxicity; real-world data; electronic health records; precision oncology; foundation models; large language models.

Article Info

Received: 05 January 2026, received in revised form: 15 January 2026, accepted: 20 January 2026, available online: 30 January 2026; Volume: 2; Issue: 1; Pages: 43-54.

Citation: Ram J. K., 2026. Explainable Artificial Intelligence for Predicting Cancer Treatment Toxicity in Real-World Clinical Practice. *International Journal of Multidisciplinary Research in Biotechnology, Pharmacy, Dental and Medical Sciences (IJMRBPDMS)* 2(1): 43-54.

DOI:

Introduction

Cancer remains one of the most significant global health challenges, with increasing incidence and mortality rates worldwide. Colorectal cancer represents the third most commonly diagnosed malignancy in both men and women and is considered a leading cause of cancer-related deaths globally. (2) Lung cancer is the leading cause of cancer deaths among both men and women, representing approximately 25% of cancer fatalities each year. (3) The treatment landscape for cancer has evolved dramatically, encompassing multiple modalities including surgery, chemotherapy, immunotherapy, targeted therapy, and radiotherapy.

Cancer treatment modalities, while life-saving, are frequently associated with significant toxicities that can compromise patient outcomes. Various adverse effects are caused by anticancer therapy, limiting the efficacy of chemotherapy. The precise prediction and early detection of adverse effects could result in improved efficacy of

chemotherapy and quality of life. (4) Treatment-related toxicities not only diminish patient quality of life but also necessitate dose modifications, treatment delays, or complete discontinuation, ultimately affecting survival outcomes.

The importance of early toxicity prediction cannot be overstated. Treatment inefficacy and other adverse events can lead to discontinuation or failure of treatment plans, or prematurely changing them, which results in a significant amount of physical, financial, and emotional toxicity to the patients and their families. (5) Traditional approaches to toxicity risk assessment have relied on clinical judgment, population-based risk scores, and conventional statistical models, which often fail to capture the complex, multidimensional nature of individual patient risk profiles.

In recent years, advances in artificial intelligence technology have led to the rapid clinical implementation of devices with AI technology in the medical field. More than 60 AI-equipped medical devices have already been approved by the Food and Drug Administration in the United States, and the active introduction of AI technology is considered to be an inevitable trend in the future of medicine. (6) The emergence of AI in oncology has opened new possibilities for precision medicine approaches to toxicity prediction.

Artificial intelligence has emerged as a transformative tool capable of addressing healthcare challenges by enhancing diagnostics, treatment planning, patient monitoring, and healthcare efficiency. AI's role in modern medicine spans disease detection, personalized care, drug discovery, predictive analytics, telemedicine, and wearable health technologies. (7) In the context of cancer treatment toxicity, AI-driven approaches can analyze vast amounts of heterogeneous data to identify patterns and risk factors that may not be apparent through conventional methods.

Real-world clinical data has become increasingly valuable for oncology research and clinical decision-making. Real-world evidence derived from sources such as electronic health records, administrative claims databases, patient registries, and wearable health devices provides valuable insights into treatment effectiveness and medication safety in routine clinical practice. (8) The integration of AI with real-world data sources represents a paradigm shift in how clinicians approach toxicity risk assessment and patient management.

Machine learning models analyze historical and real-world data to optimize eligibility criteria, simulate *in silico* cohorts, flag protocol risks, and recommend real-time adaptations. Natural language processing enhances patient screening by extracting patient data from electronic health records to match diverse patient populations to trials faster than traditional methods. (9) This review aims to comprehensively examine the current state of AI-driven cancer treatment toxicity prediction, focusing on methodological approaches, clinical applications, challenges, and future perspectives.

2. Cancer Treatment Toxicity: Clinical Significance and Challenges

2.1 Chemotherapy Toxicity

Chemotherapy remains a cornerstone of cancer treatment but is associated with substantial toxicity profiles that vary based on agent, dose, and patient characteristics. Patients with multi-adverse events had worse therapeutic efficacy of neoadjuvant chemotherapy and worse prognosis compared with patients without multi-adverse events. (4) The spectrum of chemotherapy-induced toxicities encompasses hematological, gastrointestinal, neurological, and organ-specific adverse effects.

Oxaliplatin is widely used in colorectal cancer treatment, but its dose-limiting toxicity is chemotherapy-induced peripheral neuropathy, a debilitating condition that may persist long-term and impair quality of life. Current management strategies, such as dose reduction or discontinuation, are largely empirical. (10) The unpredictable nature of individual patient responses to chemotherapy necessitates improved predictive models for personalized treatment planning.

The main adverse effects of ifosfamide, actinomycin D and vincristine treatment for rhabdomyosarcoma are haematological toxicities such as neutropenia or thrombocytopenia. The severity of these effects vary among patients but their dynamic profiles are similar. (11) Understanding the temporal dynamics of toxicity development is crucial for implementing preventive strategies.

2.2 Immunotherapy-Related Adverse Events

Immune checkpoint inhibitors have revolutionized cancer treatment but present unique toxicity challenges. Immune-related adverse events secondary to treatment with immune checkpoint inhibitors pose a major challenge in cancer treatment. Although immune-related adverse events result in substantial morbidity, there is still no reliable tool for predicting these events based on pre-treatment clinical and laboratory data. (12)

Despite the widespread use of immune checkpoint inhibitors improving survival outcomes in non-small cell lung cancer patients, immune-related adverse events triggered by ICIs have become a major challenge in clinical practice. (13) The spectrum of immune-related adverse events includes pneumonitis, dermatological reactions, colitis, hepatitis, and endocrinopathies.

Immune checkpoint inhibitors improved outcomes in NSCLC treatment, but cause immune-related adverse events. Serum proteomic biomarkers combined with clinical data may offer a better approach for toxicity risk prediction.

(14) The development of predictive biomarkers and models for immune-related toxicities represents an active area of research.

2.3 Targeted Therapy Toxicities

Targeted therapies, while more selective than conventional chemotherapy, are associated with distinct toxicity profiles. Tepotinib is approved for the treatment of patients with non-small-cell lung cancer harboring MET exon 14 skipping alterations. While edema is the most prevalent adverse event and a known class effect of MET inhibitors including tepotinib, there is still limited understanding about the factors contributing to its occurrence. (15)

Tyrosine kinase inhibitors are prescribed for chronic myeloid leukemia and some other cancers. Adverse events of small molecule kinase inhibitors at therapeutic doses in cancer patients are largely unpredictable in phase I-III studies and clinical use, despite extensive preclinical toxicity testing under good laboratory practice conditions. (16) The complex relationship between drug targets, off-target effects, and individual patient factors necessitates sophisticated predictive approaches.

2.4 Radiotherapy Toxicity

Radiation-induced toxicities represent a significant concern in cancer treatment. In order to limit radiotherapy-related side effects, effective toxicity prediction and assessment schemes are essential. Several researchers have demonstrated the high performance of ML-based models in predicting toxicity, but the application of these approaches in clinics is still lagging, partly due to their low interpretability. (17)

Radiation-induced acute skin toxicity is considered a common side effect of breast radiation therapy. (18) Additionally, one possible adverse effect of breast irradiation is the development of pulmonary fibrosis. (19) These delayed effects can significantly impact long-term quality of life.

2.5 Hematological and Organ-Specific Toxicities

Hematological toxicities remain among the most common treatment-limiting adverse effects. The most frequently reported adverse events in patients with early breast cancer were hematologic complications, affecting 87.4% of patients with gBRCAm and 63.9% of patients with non-gBRCAm, predominantly neutropenia and thrombocytopenia. (20)

Acute hematologic toxicity is a prevalent adverse tissue reaction observed in cervical cancer patients undergoing chemoradiotherapy, which may lead to various negative effects such as compromised therapeutic efficacy and prolonged treatment duration. (21) Accurate prediction of hematological toxicity can enable proactive management strategies.

Cardiotoxicity represents another significant concern. The growing awareness of cardiovascular toxicity from cancer therapies has led to the emerging field of cardio-oncology, which centers on preventing, detecting, and treating patients with cardiac dysfunction before, during, or after cancer treatment. Early detection and prevention of cancer therapy-related cardiac dysfunction play important roles in precision cardio-oncology. (22)

2.6 Limitations of Conventional Risk Prediction Models

Traditional approaches to toxicity risk assessment have significant limitations. Predictive models integrating patient-specific clinical and comorbidity data are lacking. (10) Conventional models often rely on population-averaged risk estimates that fail to account for individual patient heterogeneity and the complex interactions between patient factors, disease characteristics, and treatment regimens.

3. Real-World Clinical Data in Oncology

3.1 Electronic Health Records

Electronic health records represent a foundational data source for AI-driven toxicity prediction. Databases that link molecular data to clinical outcomes can inform precision cancer research into novel prognostic and predictive biomarkers. However, outside of clinical trials, cancer outcomes are typically recorded only in text form within electronic health records. (23)

Manual abstraction of real-world data from unstructured health records remains resource-intensive, error-prone, and highly variable across institutions. Large language models offer a scalable alternative, but their performance in multicenter oncology settings is not fully validated. (24) The challenge of extracting structured information from unstructured clinical narratives has driven innovation in natural language processing applications.

Data stored within electronic health records offer a valuable source of information for real-world evidence studies in oncology. However, many key clinical features are only available within unstructured notes. (25) Advanced AI methods are increasingly capable of extracting clinically relevant information from these unstructured sources.

3.2 Cancer Registries and Claims Databases

Population-level data sources provide complementary perspectives on treatment patterns and outcomes. Real-world

data provide essential insights into the effectiveness and safety of breast cancer treatments, particularly in diverse patient populations, where traditional clinical trials may have limitations. (26) These data sources enable large-scale analyses that can identify patterns not apparent in smaller clinical cohorts.

Social determinants of health are both drivers of health disparities and barriers to clinical research participation, particularly among historically underserved or marginalized populations. Using real-world data, diversity plans in cancer clinical trials frequently aim to reduce disparities and improve representation. (27)

3.3 Genomic Databases

Genomic information provides crucial insights into individual patient risk profiles. In locally advanced cervical cancer, phosphatidylinositol 3-kinase/serine/threonine kinase pathway is related to the occurrence of chemotherapeutic toxicity. (28) Integration of pharmacogenomic data with clinical information enhances predictive model performance.

Over the past two decades, Next-Generation Sequencing has revolutionized the approach to cancer research. Applications of NGS include the identification of tumor-specific alterations that can influence tumor pathobiology and also impact diagnosis, prognosis and therapeutic options. (29)

3.4 Patient-Reported Outcomes

Patient-reported outcomes provide essential perspectives on treatment toxicity that may not be captured through conventional clinical assessments. Patient-generated health data, or health-related data gathered from patients to help address a health concern, are used increasingly in oncology to make regulatory decisions and evaluate quality of life. Patient-generated health data include self-reported health and treatment histories, patient-reported outcomes, and biometric sensor data. (30)

Digital health provides solutions that capture patient-reported outcomes and allows symptom monitoring and patient management. The digital health solutions collecting PROs address many unmet needs, including access to care and reassurance, increase in adherence and treatment efficacy, and decrease in hospitalizations. (31)

3.5 Wearable Devices and Remote Monitoring

Wearable technologies offer continuous physiological monitoring capabilities. This prospective observational cohort study included patients with various cancer types receiving systemic anticancer treatment. Physical activity was monitored continuously using patients' own smartphones, measuring daily step count for 90 days during treatment. (32)

Wearable devices combined with artificial intelligence present an innovative solution for continuous, real-time health-related quality of life monitoring. While deep learning models effectively capture temporal patterns in physiological data, most existing approaches are unimodal, limiting their ability to address patient heterogeneity and complexity. (33)

3.6 Advantages and Limitations of Real-World Data

In a multicenter setting, AI pipelines yielded lower error rates and greater consistency than manual abstraction. These findings support the feasibility of next-generation, AI-enabled multicenter studies to generate high-quality real-world data at scale, with potential applicability in prospective clinical trials. (24)

However, challenges persist. Data quality assessments were deliberately performed for only 14.2% of structured datasets and 11.3% of unstructured datasets before model construction. Class imbalance and data fairness were the most common limitations in data quality for both types of datasets. (34)

4. Artificial Intelligence Approaches for Toxicity Prediction

4.1 Machine Learning Models

4.1.1 Random Forest

Random forest algorithms have demonstrated robust performance across multiple toxicity prediction applications. The area under ROC curve values of the random forest model were 0.75, 0.74 and 0.76 for predicting myelosuppression, low albumin and hepatic impairment, respectively, and its calibration curve was found linear in the calibration range. The random forest model outperformed the other models. (4)

Among the tested machine learning algorithms, random forest achieved the highest accuracy with area under the receiver operating characteristic curve of 0.88 for both the primary and cross-validation cohorts in predicting severe immune-related hematological adverse events. (35)

The Random Forest model showed the best performance with AUROC 0.90, accuracy 0.91, and F1-score 0.91 for predicting chemotherapy-induced peripheral neuropathy. SHAP analysis highlighted cumulative chemotherapy dose, diabetes, cardiovascular disease, and polypharmacy as major predictors. (10)

4.1.2 XGBoost and Gradient Boosting Methods

Gradient boosting methods have emerged as powerful tools for toxicity prediction. Several machine learning classifiers are investigated, and three tree ensembles—random forests, XGBoost and boosted forests—are further evaluated on the validation set to fine tune learning parameters with an objective to reduce the complexity of decision trees for providing better interpretability without significantly compromising accuracy. (5)

CatBoost achieved the highest ROCAUC of 0.737 and PRAUC of 0.040 for predicting MACE-related readmissions in hospitalized patients with blood cancers. SHapley Additive exPlanations values assessed feature importance, and clustering analysis identified high-risk subpopulations. (36)

4.1.3 Support Vector Machines

Support vector machines continue to contribute to toxicity prediction applications. A machine learning model integrating the rime optimization algorithm with self-adaptive Gaussian kernel probability search and support vector machine classifier was developed. The model achieved an accuracy of 92.381% and a specificity of 96.667% in predicting the efficacy of immunotherapy combined with chemotherapy for NSCLC. (37)

4.1.4 Logistic Regression

Despite being a simpler approach, logistic regression offers advantages in interpretability. Although the neural network model performed slightly better in the test set, the logistic regression model offered superior interpretability, and its clinical net benefit was similar to that of the neural network model. The logistic regression model was ultimately selected as the optimal predictive model with AUC of 0.855 in the test set and 0.801 in the validation set. (13)

4.2 Deep Learning Models

4.2.1 Artificial Neural Networks and Convolutional Neural Networks

Deep learning architectures have demonstrated exceptional performance in complex prediction tasks. For forecasting the response of patients to chemotherapy, the Convolutional Neural Networks technique is widely used. A deep learning-based patient response prediction system was developed to effectively predict the response of patients, predict prognosis and inform the treatment plans in the early stage. (38)

A convolutional neural network with multiple layers was trained to integrate both radiological and clinical data for predicting head and neck cancer radiotherapy toxicities. Integrating Jacobian determinant matrix from the 10th radiotherapy cone-beam CT showed better accuracy for each toxicity prediction: feeding tube (69.1% > 57.2%), hospitalization (75.3% > 63.1%) and radionecrosis (85.8% > 75.7%). (39)

4.2.2 Recurrent Neural Networks and LSTM

Recurrent architectures excel at capturing temporal patterns in longitudinal data. The prediction is performed by Multi-scale Dilated Ensemble Network, where LSTM, Recurrent Neural Network and One-dimensional Convolutional Neural Networks were integrated. The final prediction scores are averaged to develop an effective model to predict the patient's response. (38)

A multimodal deep learning approach was introduced to estimate health-related quality of life in advanced cancer patients. Physiological data collected via wearable devices are analyzed using a hybrid model combining convolutional neural networks and bidirectional long short-term memory networks with an attention mechanism. (33)

4.2.3 Transformer Architectures

Transformer-based models represent the cutting edge of deep learning in oncology. A new transformer-based pipeline for end-to-end biomarker prediction from pathology slides was developed by combining a pre-trained transformer encoder with a transformer network for patch aggregation. The transformer-based approach substantially improves the performance, generalizability, data efficiency, and interpretability as compared with current state-of-the-art algorithms. (40)

The BR-Mix3DNet model, which integrates MLP Mixer layers with 3D convolutional neural network layers, achieved a mean AUROC of 0.89 and a Youden Index of 0.68 for predicting neoadjuvant chemotherapy responsiveness in triple-negative breast cancer, outperforming other hybrid models and standalone 3D CNN models. (41)

4.3 Generative AI and Foundation Models

4.3.1 Large Language Models

Large language models are increasingly applied to clinical prediction tasks. Large language models excel on standardized oncology exams; however, their broader clinical utility remains unclear. Prompting LLMs performed similarly to engineered tabular machine learning models for predicting several adverse events, despite using only raw text from notes. (42)

Large language models have demonstrated emergent human-like capabilities in natural language processing, leading to enthusiasm about their integration in healthcare environments. In oncology, where synthesising complex, multimodal data is essential, LLMs offer a promising avenue for supporting clinical decision-making, enhancing patient care, and accelerating research. (43)

The RT-Surv framework integrates general-domain, open-source large language models to structure unstructured electronic health records alongside structured clinical data. Incorporating LLM-structured clinical features improved the concordance index from 0.779 to 0.842 during external validation. (44)

4.3.2 Clinical Foundation Models

A pan-cancer foundation model was developed trained on large-scale real-world electronic health record data. The model contains more than 1.3 billion trainable parameters and achieved high predictive performance across tasks, with test-set mortality prediction achieving AUC of 0.84-0.86 across all cancer types. (45)

The Multimodal transformer with Unified maSKed modeling (MUSK) is a vision-language foundation model designed to leverage large-scale, unlabelled, unpaired image and text data. MUSK was pretrained on 50 million pathology images and one billion pathology-related text tokens, showing strong performance in outcome prediction including immunotherapy response prediction. (46)

Virchow, the largest foundation model for computational pathology, enables pan-cancer detection, achieving 0.95 specimen-level area under the curve across nine common and seven rare cancers. With less training data, the pan-cancer detector built on Virchow can achieve similar performance to tissue-specific clinical-grade models. (47)

4.3.3 Multimodal AI

Artificial intelligence-large language models were evaluated for extracting clinical information and improving image analysis for predicting five-year survival rates of patients after radical cystectomy. The combined clinical, radiomics, and deep learning model achieved AUCs of 0.87-0.89 using GPT-4.0 extracted information. (48)

4.4 Model Explainability and Interpretability

The clinical adoption of AI models requires interpretable outputs. Sensitivity, specificity, and the area under the receiver operating characteristic curve were calculated to evaluate the classification performance of the models. SHAP values were used to perform interpretability analysis on the best model to enhance the transparency and practicality of the model. (49)

Machine learning-based approaches were applied to predict the likelihood of occurrence of edema in patients undergoing tepotinib treatment. The use of ML explainability methods identified serum albumin as the most informative longitudinal covariate, and higher age as associated with higher probabilities of more severe edema. (15)

5. Current Applications in Predicting Cancer Treatment Toxicity

5.1 Chemotherapy Toxicity Prediction

Multiple studies have demonstrated the utility of AI for chemotherapy toxicity prediction. Machine learning algorithms, including random forest, multilayer perceptron and AdaBoost, were employed to develop prediction models for common adverse effects using dynamic treatment information. A total of 1,659 chemotherapeutic information data points for 403 patients with NSCLC who underwent chemotherapy were extracted from an electronic health record system. (4)

A machine learning analysis using a gradient boosting regression technique was developed to forecast ifosfamide-induced haematological toxicities as a function of neutrophils and platelets initial levels and the initial ifosfamide dose. Among all cycles, the mean absolute errors between predicted and observed neutrophils and platelets levels were 1.0 and 72.8 G/L, respectively. (11)

A random forest machine learning model was employed to forecast neoadjuvant chemotherapy toxicity (neurological, gastrointestinal, and hematological reactions) in locally advanced cervical cancer. The Mean Decrease in Impurity approach was adopted to evaluate the relevance of selected genotypes' importance by comparing chemotherapy toxicity grades. (28)

5.2 Immune-Related Adverse Event Prediction

Machine learning algorithms have emerged as a powerful tool in cancer research, offering new opportunities to analyze complex, multidimensional data and uncover patterns that can enhance prediction. The model with the best performance was Random Forest classifier with an AUC of 0.64, specificity of 0.63 and sensitivity of 0.70 for predicting immune-related adverse events. (12)

Clinical natural language processing enables scalable, real-world detection of immune-related adverse events from unstructured EHR narratives. NLP-detected irAEs occurred in 18.8% of ICI-treated patients and were strongly associated with ICI exposure with hazard ratio of 23.72. (50)

Three machine learning models (XGBoost, HistGradientBoosting, and logistic regression) were evaluated for predicting five irAE types at multiple time points. The HistGradientBoosting model achieved superior performance with AUC of 0.75 for overall irAE prediction at 9 months using both proteomics and clinical features. (14)

5.3 Radiation Toxicity Prediction

Dosimetrics-based machine learning models were designed for prediction of acute skin toxicity. By employing the Extra Tree classifiers, the DOS+DVH+PTR model achieved a statistically significant improved performance in terms of AUC (0.83), accuracy (0.70), precision (0.74) and sensitivity (0.72) compared to other models. (18)

Planning CT scans were assessed to predict which patients are more likely to develop lung lesions after breast irradiation treatment. Three different classification methods showed predictive values above 60%, and a mathematical predictive model further strengthened the association between lung Hounsfield unit metrics and radiation-induced lung injury. (19)

A comprehensive model combining the radiomics features as well as the demographic, clinical, and dosimetric features was constructed to classify patients exhibiting acute hematologic toxicity symptoms. Bone marrow exhibited the best performance in classifying acute HT with AUC of 0.779 in the chemoradiotherapy group. (21)

5.4 Hospitalization Risk Prediction

Machine learning models were created using physical activity data from smartphones to predict adverse events. Unplanned hospitalizations in the upcoming 7 days could be predicted with high accuracy using random forest (AUC = 0.88), neural network (AUC = 0.84), and elastic net (AUC = 0.83). (32)

Machine learning approaches were developed to predict 90-day unplanned readmissions for major adverse cardiovascular events in hospitalized patients with blood cancers. Four leading predictive features were consistently identified across algorithms, including older age, heart failure, coronary atherosclerosis, and cardiac dysrhythmias. (36)

5.5 Cardiotoxicity Prediction

Classification models were trained and evaluated for 6 types of cardiovascular outcomes, including coronary artery disease (AUROC 0.821), atrial fibrillation (AUROC 0.787), heart failure (AUROC 0.882), stroke (AUROC 0.660), myocardial infarction (AUROC 0.807), and de novo CTRCD (AUROC 0.802). Model inspection revealed several clinically relevant variables significantly associated with CTRCDs, including age, hypertension, glucose levels, left ventricular ejection fraction, creatinine, and aspartate aminotransferase levels. (22)

An intelligent computational framework integrating graph neural networks and deep reinforcement learning achieved 92.3% accuracy in predicting doxorubicin-induced myocardial injury with AUC of 0.957, representing a 15.7 percentage point improvement over traditional methods. (51)

5.6 Neutropenia and Hematological Toxicity Prediction

A simple machine learning model was developed for predicting immune-related hematological adverse events associated with PD-1/PD-L1 inhibitors. Parsimonious models reduced to 50% feature importance values of the full models showed comparable performance to the full models with AUROC 0.83-0.86. (35)

Toxicity prediction studies in paediatric haematological malignancies reported high accuracy with AUC scores from 0.870 to 0.927. Significant heterogeneity was noted in ML tasks, reporting formats, and effect measures across studies, highlighting a lack of standardised reporting. (52)

5.7 Personalized Toxicity Risk Stratification

Explainable artificial intelligence was combined with multimodal real-world data to introduce AI-derived markers for clinical decision support. The approach was used to decode the outcome of 15,726 patients across 38 solid cancer entities based on 350 markers, including clinical records, image-derived body compositions, and mutational tumor profiles. (53)

The identification of biomarkers plays a crucial role in personalized medicine, both in the clinical and research settings. Various statistical and machine learning approaches have been developed to address the contrast between predictive and prognostic biomarkers. (54)

6. Challenges, Ethical Issues, and Regulatory Considerations

6.1 Data Quality and Missing Data

Data quality was infrequently assessed before the construction of ML models in head and neck cancer irrespective of the use of structured or unstructured datasets. Class imbalance reduced the discriminatory performance for models based on structured datasets while higher image resolution and good class overlap resulted in better model performance using unstructured datasets. (34)

Several challenges remain in the effective implementation of AI-enabled real-world evidence, including issues

related to data quality, interoperability between healthcare systems, algorithm transparency, and patient privacy. The transition of multiomics research to real clinics still requires consistent efforts in standardizing omics data collection and analysis. (55)

6.2 Bias and Fairness

Despite their high accuracy, ML models for predicting post-surgical readmissions can reinforce existing healthcare disparities. The best-performing model showed disparities in prediction rates across racial groups, since the model disproportionately flagged Hispanic patients for readmission risk while potentially under-identifying risk in other groups. (56)

Hope that AI will revolutionize health care delivery and improve clinical outcomes has been accompanied by concerns about the impact of these technologies on health equity. Gaps in the literature included a lack of discussion of problems of bias in AI algorithms. (57)

6.3 Explainable AI Requirements

Several researchers have demonstrated the high performance of ML-based models in predicting toxicity, but the application of these approaches in clinics is still lagging, partly due to their low interpretability. (17)

Explainable artificial intelligence is essential to enhance clinician adoption and patient outcomes in different clinical settings. Scholars note that to make AI human-centric, promote cooperation between clinicians and algorithms, and provide the transparency of data, researchers need to design AI in a more human-centric manner. (58)

6.4 Generalizability Concerns

The clinical applicability of ML models remains limited by the lack of external validation and methodological heterogeneity. Addressing these challenges through standardised reporting and rigorous external validation is needed to translate ML from a promising research tool into a reliable clinical practice component. (52)

Our participants emphasized obstacles related to molecular data access, clinical utility, and guidelines. The availability of reliable and well-curated data to train and validate machine learning algorithms and integrate multiple data sources were described as constraints yet necessary for future clinical implementation. (59)

6.5 Privacy and Regulatory Challenges

Without interpretability or transparency, AI "black boxes" risk undermining trust, raising safety concerns, and impeding regulatory acceptance. Regulators such as the U.S. Food and Drug Administration are evolving guidance frameworks that emphasize credibility, life-cycle management, and documentation. (60)

Rapid adoption is outpacing validation and governance. Inherent risks such as hallucinations, lack of explainability, spending inflation, and clinical de-skilling pose significant threats, potentially eroding trust and patient safety. (61)

Despite advances, regulatory adoption in digital pathology has lagged; to date, only three AI/ML Software as a Medical Device tools have received FDA clearance, highlighting a validation dataset gap rather than an absence of regulatory pathways. (62)

7. Future Perspectives

7.1 Federated Learning

Federated learning is advancing cancer research by enabling privacy-preserving collaborative training of machine learning models on diverse, multi-centre data. FL outperformed centralised ML in 15 out of 25 studies, spanning diverse models and clinical applications, including multi-modal integration for precision medicine. (63)

Distributed learning resulted in a reliable strategy for model development; it performed equally to models trained on centralized datasets. Sensitive data can get preserved since they are not shared for model development, constituting a promising solution for ML-based research and practice. (64)

The use of federated learning, an approach to decentralized machine learning model training, can support digital twins' performance for clinical applications. The combination of the two could alleviate privacy concerns while bolstering machine learning model performance and resulting predictions. (65)

7.2 Multimodal Oncology AI

This vision paper outlines a strategic initiative to harness multi-modal AI, federated deep learning and confidential computing for precision oncology. By integrating multi-omic and multi-scale data—including genomic, proteomic, radiomic, imaging, pathology, and clinical biomarkers—an AI-driven framework can accurately stage cancer progression and predict optimal treatment cocktails. (66)

The integration of multi-omics data, spanning genomics, transcriptomics, proteomics, metabolomics and radiomics, can improve diagnostic and prognostic accuracy. Cutting-edge AI methodologies include graph neural networks for biological network modeling, transformers for cross-modal fusion, and explainable AI for transparent clinical decision support. (67)

7.3 Digital Twins

The emergence of digital twin technology represents a paradigm shift in precision oncology, offering unprecedented opportunities to transform how we diagnose, treat, and monitor cancer patients. In personalized treatment planning, they enable simulation of tumor responses across treatment modalities—immunotherapy, chemotherapy, radiation—allowing clinicians to develop bespoke treatment plans that optimize outcomes while minimizing adverse effects. (68)

A novel framework for Cancer Patient Digital Twins aims to enhance predictive analytics, treatment optimization, clinical decision-making, and oncology outcomes through the integration of AI-driven data fusion and real-time monitoring. The CPDT framework combines advanced technologies such as deep learning, federated learning, complex biological simulations, and quantum-assisted computing. (69)

TWIN-GPT, a large language model-based digital twin creation approach, can establish cross-dataset associations of medical information given limited data, generating unique personalized digital twins for different patients, thereby preserving individual patient characteristics. (70)

7.4 Foundation Models and Precision Oncology

Artificial intelligence is reshaping oncology by extracting clinically actionable signals from complex cancer data and accelerating drug development. Emerging directions include multimodal foundation models, federated learning, AI stewardship, and patient-specific digital twins. (71)

Applications of AI/ML in precision oncology are extensive and include the generation of synthetic data, e.g., digital twins, in order to provide the necessary information to design or expedite the conduct of clinical trials. (72)

7.5 Real-Time Toxicity Monitoring

An AI-driven digital twin framework for personalized therapeutic optimization demonstrated 30–40% improvement in treatment efficacy, with chemotherapy resistance predicted at 92% accuracy and a 40% reduction in hospital readmissions through early anomaly detection. (73)

AI-driven analysis of data from electronic wearables and imaging enables early toxicity and efficacy signals, allowing providers real-time monitoring. (9)

8. Conclusion

The integration of artificial intelligence with real-world clinical data represents a transformative advancement in cancer treatment toxicity prediction. The role of machine learning in the diagnosis and treatment of various types of oncology is steadily increasing. It is expected that the use of AI in oncology will speed up both diagnostic and treatment planning processes. (74)

This review has demonstrated that machine learning and deep learning approaches, from traditional algorithms such as random forest and XGBoost to advanced transformer architectures and foundation models, can effectively predict diverse treatment-related toxicities across multiple cancer types and treatment modalities. The performance of the ML models was generally strong, with an average area under the curve of 76.68%, demonstrating the potential of these approaches for clinical application. (1)

Real-world clinical data sources, including electronic health records, genomic databases, and wearable devices, provide rich information for developing personalized risk prediction models. AI-driven predictive modelling techniques, including machine learning and natural language processing, enable the identification of treatment patterns, prediction of drug responses, and early detection of adverse drug reactions. (8)

However, significant challenges remain before widespread clinical implementation can be realized. While participants recognized the issue of hype surrounding machine learning in precision oncology, they agreed that, in an assistive role, it represents the future of precision oncology. The field must move beyond hype and toward concrete efforts to overcome key obstacles, such as ensuring access to molecular data, establishing clinical utility, developing guidelines and regulations, and meaningfully addressing ethical challenges. (59)

Future directions including federated learning, multimodal AI integration, digital twins, and foundation models hold tremendous promise for advancing personalized cancer care. Data-centric methodologies such as federated learning, differential privacy, and synthetic data generation address challenges related to data sharing and patient privacy. Rigorous benchmarking, explainable AI methods, and prospective multi-center trials are essential for validating ML tools and establishing clinician trust. (75)

In conclusion, AI-driven prediction of cancer treatment toxicity using real-world clinical data represents a rapidly evolving field with substantial potential to improve patient outcomes through early identification of at-risk individuals, personalized treatment optimization, and proactive clinical management. Continued collaboration between clinicians, data scientists, and regulatory bodies will be essential to translate these promising technologies into routine clinical practice, ultimately benefiting cancer patients worldwide.

References

1. Hanahan D. Hallmarks of cancer: new dimensions. *Cancer Discov.* 2022;12(1):31–46. Doi:10.1158/2159-8290.CD-21-1059.
2. Rajendran LKK. Machine Learning–Driven Symptom–Based Cancer Risk Stratification: A Systematic Review of Clinical Prediction Models and Methodological Rigor. *Int J Drug Deliv Technol.* 2026;16(40s):242–253. Doi:10.25258/ijddt.16.40s.26.
3. Rajendran LKK. Identifying Determinants of Outcome in Post-Radiotherapy Cervical Carcinoma Requiring Adjuvant Surgery. *International Journal of Clinical Research in Medical Sciences.* 2026;1(2):1–10. Doi:10.67231/3acej759.
4. Kumar RMH. Pan-System Cancer Intelligence: Integrating Blood, Immune, Microbiome, and Tumor Microenvironment Data Using Foundation Models. *Power System Protection and Control.* 2023;51(4):92–100. Doi:10.46121/pspc.51.4.8.
5. Maradi Hemanth Kumar R. AI-Driven Liquid Biopsy Systems for Early Cancer Detection and Personalized Oncology. *Power System Protection and Control.* 2023;51(4):66–83. Doi:10.46121/pspc.51.4.7.
6. Rajendran LKK. Hematological Malignancy Identification via K-means based ROI Extraction. *International Journal of Clinical Research in Medical Sciences.* 2026;1(2):1–10. Doi:10.67231/kt1w3e73.
7. Rajendran OK. Bias, Fairness, and Ethical Challenges in Artificial Intelligence: A Comprehensive Review of Causes, Impacts, and Mitigation Strategies. *Scientific Culture.* 2026;12(2.1):13001–13010. Doi:10.5281/zenodo.20374091.
8. Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. *Nat Med.* 2019;25(1):44–56. Doi:10.1038/s41591-018-0300-7.
9. Rajendran OK. Clinical Translation of Artificial Intelligence in Oncology: Real-World Validation, Workflow Integration, and Precision Medicine Applications. *Int J Drug Deliv Technol.* 2026;16(49s):956–964. Doi:10.25258/ijddt.16.49s.110.
10. Rajendran LKK. Interpretable Machine Learning for Early Mortality Prediction in Acute Myeloid Leukemia: A Decision Tree–Based Retrospective Cohort Study. *Int J Drug Deliv Technol.* 2026;16(40s):231–241. Doi:10.25258/ijddt.16.40s.25.
11. Esteva A, Robicquet A, Ramsundar B, et al. A guide to deep learning in healthcare. *Nat Med.* 2019;25(1):24–29. Doi:10.1038/s41591-018-0316-z.
12. Rajendran OK. Generative AI for Synthetic Medical Image Generation in Oncology: Addressing Data Scarcity in AI-Driven Cancer Diagnosis. *Int J Drug Deliv Technol.* 2026;16(49s):1010–1016. Doi:10.25258/ijddt.16.49s.117.
13. Rajendran LKK. Integrated Prognostic Modeling of Tumor Stage, Multimodal Therapy, and Functional Status in Lung Cancer Survival: A Real-World Cohort Study. *Scientific Culture.* 2026;12(5):567–576. Doi:10.5281/zenodo.1250046.
14. Bommasani R, Hudson DA, Adeli E, et al. On the opportunities and risks of foundation models. *arXiv.* 2021. Doi:10.48550/arXiv.2108.07258.
15. Rajendran LKK. Integrative Pharmacogenomic Analysis of Drug Response Heterogeneity Across Cancer Cell Lines: Insights From Large-Scale GDSC Data. *Scientific Culture.* 2026;12(4):7537–7546. Doi:10.5281/zenodo.12426762.
16. 16.Acs B, Rantalainen M, Hartman J. Artificial intelligence as the next step towards precision pathology. *J Intern Med.* 2020;288(1):62–81. Doi:10.1111/joim.13030.
17. Rajendran OK. Tumor Microenvironment Interaction-Guided Graph Neural Networks for Survival Prediction from Whole-Slide Pathology Images. *Int J Drug Deliv Technol.* 2026;16(49s):481–488. Doi:10.25258/ijddt.16.49s.50.
18. Rajendran LKK. Evaluating the Association of Cancer-Related Risk Factors With Multisystem Health: Insights Into Fertility, Cardiovascular, and Renal Indicators. *Scientific Culture.* 2026;12(4):7520–7527. Doi:10.5281/zenodo.12426760.
19. Rajendran LKK. From Prediction to Precision: An Externally Validated Deep Learning–Based Survival and Adjuvant Therapy Recommendation System for Resected Stage III Non–Small Cell Lung Cancer. *Int J Drug Deliv Technol.* 2026;16(30s):430–438. doi:10.25258/ijddt.16.30s.41.
20. Chen RJ, Lu MY, Wang J, et al. Pathomic fusion: an integrated framework for fusing histopathology and genomic features for cancer diagnosis and prognosis. *Nat Mach Intell.* 2022;4:179–193. Doi:10.1038/s42256-022-00466-x.
21. Rajendran LKK. From Prediction to Practice: A Machine Learning–Based Clinical Decision Support Tool for Bevacizumab Risk Stratification in Oncology. *Int J Drug Deliv Technol.* 2026;16(30s):414–429. Doi:10.25258/ijddt.16.30s.40.
22. Rajendran OK. Self-supervised multimodal Learning for early cancer detection across Imaging and genomics. *Power System Protection and Control.* 2024;52(4):167–178. Doi:10.46121/pspc.52.4.14.

23. Rajendran OK. Explainable AI-Driven Clinical. Decision Support Systems in Precision Oncology: Interpretable Models for Multimodal Cancer Care. *Scientific Culture*. 2026;12(2.1):12359-12369. Doi:10.5281/zenodo.20328194.
24. Rajendran LKK. Impact of Treatment Modalities on Fertility, Sexual Function, and Psychological Outcomes in Testicular Cancer Survivors: A Comprehensive Review. *Int J Drug Deliv Technol*. 2026;16(30s):447-453. Doi:10.25258/ijddt.16.30s.43.
25. Rajendran LKK. Intelligent Omics-Driven Patient Stratification for Cancer Therapeutic Re-profiling. *International Journal of Clinical Research in Medical Sciences*. 2026;1(1):1-11. Doi:10.67231/gv5hck05.
26. Rajendran LKK. Cancer nanomedicine: utilizing the enhanced permeability and retention (EPR) effect to deliver high payloads of chemotherapeutic agents directly to tumor sites. *Power System Protection and Control*. 2024;52(2):123-129. Doi:10.46121/pspc.52.2.12.
27. Kather JN, Calderaro J. Development of AI in digital pathology. *Nat Rev Clin Oncol*. 2020;17(10):591–595. Doi:10.1038/s41571-020-00431-0.
28. Rajendran OK. AI-based radiogenomic Models for predicting immunotherapy response In solid tumors. *Power System Protection and Control*. 2023;51(4):24-37. Doi:10.46121/pspc.51.4.4.
29. Rajendran LKK. Enhanced Predictive Analytics for Early Malignancy Discovery in Routine Screening. *International Journal of Clinical Research in Medical Sciences*. 2026;1(1):1-10. Doi:10.67231/grams870.
30. Wan JCM, Massie C, Garcia-Corbacho J, et al. Liquid biopsies come of age: towards implementation of circulating tumour DNA. *Nat Rev Cancer*. 2017;17(4):223–238. Doi:10.1038/nrc.2017.7.
31. Rajendran OK. Machine Learning-Based Prediction of Chemotherapy Toxicity in Colorectal Cancer: A Personalized Risk Stratification Approach. *Scientific Culture*. 2026;12(5.1):942-952. Doi:10.5281/zenodo.12511075.
32. Rajendran OK. Federated radiology AI Models for multi-institutional cancer diagnosis Without data sharing. *Power System Protection And Control*. 2023;51(4):38-54. Doi:10.46121/pspc.51.4.5.
33. Bera K, Schalper KA, Rimm DL, et al. Artificial intelligence in digital pathology — new tools for diagnosis and precision oncology. *Nat Rev Clin Oncol*. 2019;16(11):703–715. Doi:10.1038/s41571-019-0252-y.
34. Rajendran OK. Deep Reinforcement Learning in Oncology: Advances in Cancer Imaging, Radiotherapy, and Personalized Treatment. *Scientific Culture*. 2026;12(5):597-606. Doi:10.5281/zenodo.1250048.
35. Rajendran OK. DEEP LEARNING FOR CROSS-MODALITY MAPPING BETWEEN HISTOPATHOLOGY AND RADIOLOGICAL IMAGING. *Power System Protection and Control*. 2025;53(3):313-328. Doi:10.46121/pspc.53.3.21.
36. Lu MY, Chen TY, Williamson DFK, et al. AI-based pathology predicts origins for cancers of unknown primary. *Nature*. 2021;594(7861):106–110. Doi:10.1038/s41586-021-03512-4.
37. Rajendran OK. Artificial Intelligence in Oncologic Imaging: Deep Learning, Radiomics, and Clinical Integration for Precision Cancer Diagnosis. *Int J Drug Deliv Technol*. 2026;16(50s):871-880. Doi:10.25258/ijddt.16.50s.92.
38. Bilal M, Raza SEA, Azam A, et al. Development and validation of a weakly supervised deep learning framework to predict the risk of colorectal cancer recurrence from histology images. *Lancet Oncol*. 2021;22(11):153–163. Doi:10.1016/S1470-2045(21)00430-5.
39. Rajendran OK. DIGITAL TWIN FRAMEWORKS FOR PERSONALIZED CANCER PROGRESSION MODELING USING LONGITUDINAL DATA. *Power System Protection and Control*. 2025;53(4):486-501. Doi:10.46121/pspc.53.4.33.
40. Rajendran LKK. Genomic profiling: utilizing Multi-omics data to identify potential Therapeutic targets and resistance markers. *Power System Protection and Control*. 2024;52(4):159-166. Doi:10.46121/pspc.52.4.13.
41. Rajendran OK. Artificial Intelligence–Driven Multimodal Imaging for Cancer During Pregnancy: Advances in Maternal–Fetal Diagnostics and Precision Oncology. *Int J Drug Deliv Technol*. 2026;16(50s):862-870. Doi:10.25258/ijddt.16.50s.91.
42. Rajendran LKK. Immunotherapy and cell Therapy: developing CAR-T cell therapies and Other immune-based treatments for cancer and Autoimmune diseases. *Power System Protection and Control*. 2023;51(2):64-77. Doi:10.46121/pspc.51.2.7.
43. Rajendran OK. FOUNDATION MODEL–DRIVEN PRECISION ONCOLOGY: INTEGRATING MULTI-OMICS, RADIOLOGY, AND CLINICAL DATA FOR PREDICTIVE CANCER CARE. *Power System Protection and Control*. 2024;52(2):154-163. Doi:10.46121/pspc.52.2.14.
44. Rajendran LKK. Theranostics: integrating Diagnostic imaging agents and therapeutic Drugs into a single multifunctional nano-Platform for real-time monitoring of treatment. *Power System Protection and Control*. 2025;53(2):376-386. Doi:10.46121/pspc.53.2.31.
45. Rajendran LKK. Mechanisms driving Immunotherapy resistance in colorectal cancer Liver metastases. *Power System Protection and Control*. 2024;52(1):29-37. Doi:10.46121/pspc.52.1.5.
46. Ching T, Himmelstein DS, Beaulieu-Jones BK, et al. Opportunities and obstacles for deep learning in biology

- and medicine. *J R Soc Interface*. 2018;15(141):20170387. Doi:10.1098/rsif.2017.0387.
47. Litjens G, Kooi T, Bejnordi BE, et al. A survey on deep learning in medical image analysis. *Med Image Anal*. 2017;42:60–88. Doi:10.1016/j.media.2017.07.005.
 48. Hemanth Kumar RM. Integrated Transcriptomic and 3 Learning Framework Identifies a Blood-Based Biomarker Signature for Anthracycline-Induced Cardiotoxicity in Juvenile Cancer Survivors. *Int J Drug Deliv Technol*. 2026;16(40s):219-230. Doi:10.25258/ijddt.16.40s.24.
 49. Mobadersany P, Yousefi S, Amgad M, et al. Predicting cancer outcomes from histology and genomics using convolutional networks. *Proc Natl Acad Sci USA*. 2018;115(13):E2970–E2979. Doi:10.1073/pnas.1717139115.
 51. Lambin P, Leijenaar RTH, Deist TM, et al. Radiomics: the bridge between medical imaging and personalized medicine. *Nat Rev Clin Oncol*. 2017;14(12):749–762. Doi:10.1038/nrclinonc.2017.141.
 52. Azizi S, Mustafa B, Ryan F, et al. Big self-supervised models advance medical image classification. *Nature*. 2021;594(7864):104–110. Doi:10.1038/s41586-021-03476-6.
 53. Dosovitskiy A, Beyer L, Kolesnikov A, et al. An image is worth 16×16 words: transformers for image recognition at scale. *arXiv*. 2020. Doi:10.48550/arXiv.2010.11929.
 54. Rajendran OK. DeepDRA: A Deep Learning Framework for Drug Repurposing and Cancer Drug Response Prediction Using Multi-Omics Data. *Scientific Culture*. 2026;12(3):68-77. Doi:10.5281/zenodo.12326001.
 55. Xu H, Usuyama N, Bagga J, et al. A whole-slide foundation model for digital pathology from real-world data. *Nature*. 2024;630(8015):181–188. Doi:10.1038/s41586-024-07441-w.
 56. Singhal K, Azizi S, Tu T, et al. Large language models encode clinical knowledge. *Nature*. 2023;620(7972):172–180. Doi:10.1038/s41586-023-06291-2.
 57. Moor M, Banerjee O, Abad ZSH, et al. Foundation models for generalist medical artificial intelligence. *Nature*. 2023;616(7956):259–265. Doi:10.1038/s41586-023-05881-4.
 58. Chen RJ, Ding T, Lu MY, et al. Towards a general-purpose foundation model for computational pathology. *Nat Med*. 2024;30(3):850–862. Doi:10.1038/s41591-024-02857-3.
 59. Dr. Isabella Moore, Multimodal Artificial Intelligence in Oncology: Integrating Radiomics, Pathomics, and Genomics, *Int. J. of Pharm.Sci.*, 2026, Vol 4, Issue 5, 6745-6760. <https://doi.org/10.5281/zenodo.20391855>
 60. Dr. Benjamin Walker, Dr. Eleanor Hayes, Dr. Christopher Nolan, Foundation Models in Cancer Medicine: Revolutionizing Precision Diagnostics and Clinical Oncology, *Int. J. of Pharm. Sci.*, 2026, Vol 4, Issue 5, 6733-6744. <https://doi.org/10.5281/zenodo.20391588>