

Digital Twins in Cancer Care: Building Virtual Patients for Personalized Medicine

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ABSTRACT:

Cancer care is undergoing a major transformation through the convergence of artificial intelligence (AI), computational modeling, systems biology, and precision medicine. Among the most promising innovations is the development of digital twins—continuously evolving virtual representations of individual patients that integrate clinical, radiological, pathological, genomic, molecular, physiological, and longitudinal health information to simulate disease progression and therapeutic response. Unlike conventional predictive models that analyze isolated datasets, digital twins continuously incorporate newly acquired patient information, allowing personalized prediction, adaptive treatment optimization, toxicity assessment, and long-term survivorship planning. Recent advances in machine learning, deep learning, multimodal learning, transformer architectures, graph neural networks, foundation models, and generative AI have significantly enhanced the construction and clinical applicability of oncology digital twins. These intelligent computational systems are increasingly being investigated for tumor diagnosis, radiogenomics, computational pathology, immunotherapy prediction, adaptive radiation planning, surgical simulation, drug discovery, and clinical decision support. Furthermore, integration with wearable technologies, cloud computing, digital pathology, and electronic health records enables continuous updating of virtual patient models throughout the cancer journey. Despite remarkable progress, significant challenges remain regarding data standardization, interoperability, computational complexity, explainability, cybersecurity, ethical governance, regulatory validation, and clinical implementation. This review provides a comprehensive overview of digital twin technologies in cancer care, emphasizing their computational foundations, clinical applications, emerging innovations, and future role in advancing personalized medicine.[1]

Keywords: Digital twins, Precision oncology, Artificial intelligence, Personalized medicine, Computational oncology, Machine learning, Multimodal learning, Digital pathology, Clinical decision support, Virtual patients.

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Introduction

Cancer remains one of the leading causes of morbidity and mortality worldwide despite remarkable progress in molecular diagnostics, targeted therapies,

immunotherapy, and precision medicine. The biological heterogeneity of malignant tumors results from dynamic interactions among genomic alterations, epigenetic

regulation, immune responses, metabolic remodeling, and the tumor microenvironment. Consequently, patients with apparently similar pathological diagnoses frequently demonstrate markedly different therapeutic responses, recurrence patterns, and survival outcomes, illustrating the limitations of conventional population-based treatment strategies.[2]

Modern oncology increasingly depends upon enormous quantities of heterogeneous biomedical information generated through radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, laboratory investigations, wearable devices, and electronic health records. Although these diverse data sources collectively provide comprehensive insights into tumor biology, their complexity frequently exceeds the analytical capacity of conventional statistical methods and routine clinical workflows.[3]

Artificial intelligence has emerged as a transformative technology capable of integrating these multidimensional datasets into clinically meaningful knowledge. Recent advances in computational medicine have extended AI beyond isolated predictive algorithms toward continuously evolving virtual patient models known as digital twins. These systems integrate multimodal biomedical information to simulate disease progression, estimate therapeutic response, and support individualized clinical decision-making throughout the cancer care continuum.[4]

By enabling clinicians to evaluate multiple therapeutic scenarios before initiating treatment, digital twins represent one of the most promising innovations in personalized oncology. Their adaptive learning capabilities allow virtual patients to evolve alongside biological patients, providing continuously updated insights that support increasingly individualized cancer management.[5]

2. Evolution of Digital Twin Technology in Healthcare

The concept of digital twins originated within engineering and manufacturing industries, where virtual replicas of complex mechanical systems were developed to monitor operational performance, predict equipment

3. Architecture of Oncology Digital Twins

An oncology digital twin consists of multiple interconnected computational layers that continuously exchange information to maintain an up-to-date virtual representation of an individual patient. Rather than functioning as a single artificial intelligence model,

failure, and optimize maintenance strategies. Aerospace engineering pioneered many of these applications, followed by widespread adoption across automotive manufacturing, industrial automation, robotics, and smart infrastructure.[6]

The successful implementation of digital twins in engineering inspired researchers to adapt similar principles to biological systems. Instead of simulating mechanical components, healthcare digital twins model physiological processes, disease progression, therapeutic interventions, and patient-specific clinical outcomes. Early medical applications focused on cardiovascular disease, diabetes management, orthopedic biomechanics, and intensive care monitoring, where continuously collected physiological data supported predictive computational modeling.[7]

The rapid expansion of biomedical technologies—including next-generation sequencing, advanced imaging, wearable biosensors, molecular diagnostics, and cloud-based health records—accelerated development of healthcare digital twins. Artificial intelligence became essential for integrating these heterogeneous data streams into clinically meaningful predictive models capable of supporting personalized medicine.[8]

Cancer medicine emerged as one of the most suitable fields for digital twin implementation because oncology requires continuous integration of imaging, pathology, molecular biology, treatment history, and longitudinal clinical information. Every patient's tumor exhibits unique biological characteristics and evolves dynamically throughout treatment, making digital twins particularly valuable for individualized cancer management.[9]

Today, oncology digital twins extend beyond simple predictive algorithms by integrating systems biology, mathematical modeling, multimodal artificial intelligence, probabilistic inference, and mechanistic simulations into comprehensive computational ecosystems that represent the entire cancer journey from diagnosis to survivorship.[10]

digital twins integrate several complementary computational components operating simultaneously across multiple biological scales.[11]

The first layer involves acquisition of diverse patient-specific information from radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, laboratory biomarkers, physiological

monitoring, treatment records, medication history, and electronic health documentation. Each data source contributes complementary biological information regarding tumor characteristics and overall patient health.[12]

The second layer performs multimodal data harmonization. Because biomedical information originates from different technologies and formats, sophisticated preprocessing pipelines normalize molecular profiles, standardize imaging data, extract quantitative biomarkers, encode clinical narratives through natural language processing, and align heterogeneous datasets into unified computational representations.[13]

Artificial intelligence constitutes the third computational layer, where deep learning, transformer architectures, graph neural networks, and probabilistic machine learning models analyze integrated patient data to estimate disease progression, therapeutic response, toxicity risk, and survival outcomes. These computational methods generate personalized biological representations that support downstream clinical decision-making.[14]

Simulation engines represent another essential component of digital twins by modeling tumor growth kinetics, metastatic dissemination, immune interactions, therapeutic interventions, and resistance mechanisms. As new patient information becomes available, these mathematical models dynamically update disease trajectories, allowing clinicians to compare multiple treatment strategies before implementation.[15]

The final layer involves visualization and clinical decision support. Interactive dashboards display predicted disease progression, therapeutic response probabilities, toxicity estimates, recurrence risk, and personalized treatment recommendations in formats that facilitate multidisciplinary collaboration while maintaining physician oversight.[16]

5. Multimodal Data Integration

The effectiveness of oncology digital twins depends upon their ability to integrate diverse biomedical information into unified computational frameworks. Cancer is inherently multifactorial, with tumor behavior influenced by genetic alterations, epigenetic regulation, immune responses, metabolic pathways, anatomical characteristics, treatment history, and patient-specific clinical variables. Consequently, reliance on a single data source rarely captures the full biological complexity of individual malignancies.[21]

4. Artificial Intelligence Technologies Enabling Digital Twins

Artificial intelligence forms the computational foundation of modern oncology digital twins by transforming heterogeneous biomedical information into clinically actionable insights. Multiple complementary AI technologies work together to enable construction of continuously evolving virtual patient models.[17]

Machine learning algorithms initially provided the basis for predictive modeling by identifying relationships between clinical variables and patient outcomes. Random forests, support vector machines, and gradient boosting algorithms demonstrated considerable success in predicting recurrence, survival, and therapeutic response across multiple malignancies.

Deep learning significantly expanded these capabilities through automated extraction of hierarchical features from medical imaging, digital pathology, and molecular datasets. Convolutional neural networks transformed radiological interpretation, while recurrent neural networks enabled temporal analysis of longitudinal patient information.[18]

Transformer architectures have further enhanced digital twin development by efficiently processing multimodal biomedical information while preserving long-range contextual relationships. Self-attention mechanisms allow simultaneous analysis of imaging findings, genomic profiles, pathology reports, laboratory investigations, and clinical documentation to generate highly individualized patient representations.[19]

Foundation models trained on enormous biomedical datasets improve scalability by learning generalized representations that can subsequently be adapted to multiple oncology applications through transfer learning. These models reduce dependence on manually annotated datasets while improving robustness across diverse cancer types and healthcare environments.[20]

Medical imaging provides anatomical and functional information regarding tumor morphology, vascularity, metabolic activity, and disease progression. Histopathological analysis contributes microscopic assessment of tissue architecture, immune infiltration, stromal composition, and cellular differentiation. Molecular profiling identifies genomic alterations, transcriptomic signatures, proteomic pathways, and epigenetic modifications associated with prognosis and therapeutic response. Clinical information—including laboratory investigations, medications, comorbidities,

treatment history, and longitudinal follow-up—provides essential context for personalized prediction models.[22] Artificial intelligence harmonizes these heterogeneous datasets through multimodal representation learning. Advanced computational models align imaging biomarkers with molecular signatures and clinical variables, revealing biological relationships that are difficult to identify using conventional analytical approaches. This integration enables digital twins to generate increasingly accurate individualized predictions while continuously adapting as new patient information becomes available.[23]

6. Digital Twins in Cancer Diagnosis

Digital twins are increasingly being incorporated into diagnostic oncology by integrating radiological imaging, computational pathology, laboratory biomarkers, and molecular diagnostics into unified patient models. Medical imaging—including computed tomography, magnetic resonance imaging, positron emission tomography, mammography, and ultrasound—provides non-invasive assessment of tumor characteristics throughout disease progression.[24]

Artificial intelligence automatically detects tumors, segments anatomical structures, measures lesion volume, and characterizes imaging phenotypes associated with disease aggressiveness. Radiomics further enhances diagnostic precision by extracting quantitative imaging biomarkers describing tumor heterogeneity, vascularity, morphology, and spatial organization. These imaging-derived features are continuously incorporated into the digital twin, allowing the virtual patient model to evolve as treatment progresses.[25]

7. Computational Pathology and Radiogenomics

Digital pathology has become another essential component of oncology digital twins through high-resolution whole-slide imaging and AI-assisted computational analysis. Deep learning models identify subtle histopathological features associated with tumor subtype, metastatic potential, stromal remodeling, immune infiltration, angiogenesis, and therapeutic response.[26]

Artificial intelligence can also predict clinically relevant molecular alterations—including EGFR mutations,

KRAS mutations, HER2 amplification, microsatellite instability, and PD-L1 expression—directly from tissue morphology, potentially reducing dependence on expensive molecular testing while accelerating precision oncology workflows.[27]

Radiogenomics further extends digital twin capabilities by integrating quantitative imaging biomarkers with genomic sequencing and molecular profiling. These computational approaches enable non-invasive prediction of molecular characteristics using routine clinical imaging, supporting repeated assessment of tumor evolution without requiring multiple invasive biopsies.[28]

The integration of computational pathology, radiogenomics, and multimodal AI substantially enhances the biological accuracy of digital twins, improving diagnosis, prognostic prediction, and individualized treatment planning while supporting increasingly precise personalized medicine.[29]

8. Digital Twins in Immuno-Oncology

Immunotherapy has transformed the management of many malignancies; however, predicting which patients will achieve durable clinical benefit remains a major challenge. Digital twins provide a powerful framework for modeling interactions between tumor cells, immune cells, cytokine networks, and the tumor microenvironment. By integrating genomic alterations, immunomic profiles, digital pathology, radiological imaging, laboratory biomarkers, and clinical characteristics, artificial intelligence enables simulation of individualized immune responses to therapy.[1]

Machine learning algorithms quantify tumor-infiltrating lymphocytes, immune checkpoint expression, inflammatory signaling pathways, stromal barriers, and spatial organization of immune cells. These computational models estimate the probability of response to immune checkpoint inhibitors, CAR-T cell therapy, cancer vaccines, bispecific antibodies, and combination immunotherapies, supporting more precise patient selection while minimizing unnecessary toxicity.[2]

derived from population-based clinical trials, clinicians can evaluate multiple therapeutic strategies within a patient's virtual model before initiating therapy.[3]

Simulation engines estimate expected tumor response, recurrence probability, treatment-related toxicity,

progression-free survival, and overall survival under various combinations of chemotherapy, targeted therapy, immunotherapy, surgery, and radiation therapy. These virtual experiments enable comparison of treatment options while minimizing unnecessary patient risk and supporting evidence-based precision medicine.[4] Because digital twins are continuously updated with new imaging findings, laboratory investigations, molecular data, and treatment responses, therapeutic recommendations evolve alongside the patient's disease, reflecting the dynamic nature of cancer biology.

10. Adaptive Radiation Oncology

Radiation therapy remains one of the most important treatment modalities in oncology. However, tumor size, anatomical position, and surrounding healthy tissues often change during treatment, reducing the effectiveness of static radiation plans.[5]

Digital twins address these limitations by incorporating sequential imaging acquired throughout radiation therapy. Artificial intelligence automatically updates tumor contours, predicts anatomical changes, estimates radiation sensitivity, and recommends personalized treatment modifications.

These adaptive simulations enable optimization of radiation dose distribution according to the patient's evolving anatomy and biological response, improving tumor control while minimizing radiation exposure to surrounding organs.[6]

11. Surgical Planning and Intraoperative Guidance

Digital twins are increasingly being investigated for surgical oncology applications. Three-dimensional virtual models generated from multimodal imaging provide detailed visualization of tumor location, vascular anatomy, adjacent organs, and critical neurovascular structures before surgery.[7]

Artificial intelligence enhances surgical planning by predicting resection margins, estimating operative complexity, assessing postoperative complications, and modeling functional outcomes. Surgeons can evaluate multiple operative strategies within the digital twin

before entering the operating room, improving procedural planning and patient safety.

Future integration with robotic surgical systems, intraoperative imaging, and real-time physiological monitoring may enable continuously updated digital twins capable of providing dynamic guidance during surgical procedures.[8]

12. Drug Discovery and Clinical Trials

Digital twins offer important opportunities for accelerating anticancer drug development through computational simulation of therapeutic response before laboratory or clinical testing. Artificial intelligence integrates molecular biology, pharmacogenomics, systems pharmacology, and patient-specific disease models to predict drug efficacy, toxicity, resistance mechanisms, and optimal dosing strategies.[9]

Digital twins also improve clinical trial design by identifying patients most likely to benefit from investigational therapies based on individualized biological characteristics. Virtual patient cohorts may reduce recruitment requirements, improve patient stratification, and support more efficient evaluation of novel therapeutic interventions while preserving scientific rigor.[10]

13. Clinical Decision Support

Modern oncology requires continuous interpretation of enormous quantities of biomedical information generated throughout diagnosis, treatment, and follow-up. Digital twins function as intelligent clinical decision-support systems by integrating imaging studies, pathology findings, laboratory results, genomic reports, medication histories, and treatment outcomes into unified computational platforms.[11]

Interactive dashboards display individualized disease trajectories, therapeutic response probabilities, toxicity estimates, recurrence risk, and survival predictions. Rather than replacing physician expertise, these systems provide evidence-based recommendations that support multidisciplinary decision-making and improve consistency in personalized cancer care.[12]

for computational predictions rather than functioning as an opaque "black box." [13]

Visualization techniques such as saliency maps, attention heatmaps, SHAP (Shapley Additive Explanations), and counterfactual analyses identify the variables that contribute most strongly to individual predictions. These approaches allow clinicians to verify whether AI systems

14. Explainable Artificial Intelligence and Trustworthy Digital Twins

Clinical implementation of digital twins requires transparency, interpretability, and physician confidence. Explainable artificial intelligence (XAI) addresses these requirements by providing understandable explanations

are focusing on biologically meaningful features while improving multidisciplinary communication and regulatory acceptance.[14]

Transparent digital twins are expected to strengthen clinician trust, improve patient acceptance, and facilitate safe integration into routine oncology practice.

15. Privacy, Federated Learning, and Cybersecurity

Large-scale digital twin ecosystems require access to diverse clinical datasets collected across multiple healthcare institutions. Federated learning provides a privacy-preserving solution by enabling institutions to collaboratively train artificial intelligence models without transferring raw patient data.[15]

In this framework, local models are trained within individual hospitals, while only encrypted model parameters are shared and aggregated into improved global models. Additional privacy-preserving technologies—including differential privacy, homomorphic encryption, secure multi-party computation, and blockchain-based audit systems—further strengthen data security and regulatory compliance.[16]

Robust cybersecurity measures remain essential because digital twins continuously exchange information among imaging systems, pathology laboratories, genomic sequencing platforms, wearable devices, cloud infrastructure, and hospital information systems.

16. Digital Biomarkers and Remote Patient Monitoring

18. Discussion

Digital twins represent one of the most promising innovations in precision oncology because they enable dynamic, patient-specific computational modeling throughout the cancer care continuum. Unlike conventional predictive algorithms that analyze isolated datasets, digital twins continuously integrate multimodal biomedical information to simulate disease evolution, optimize treatment selection, estimate toxicity, and support long-term survivorship planning.[21]

19. Conclusion

Digital twins are redefining personalized cancer medicine by creating continuously evolving virtual representations of individual patients that integrate radiology, pathology, genomics, molecular biology, clinical information, wearable technologies, and

Wearable medical technologies and mobile health applications have expanded the scope of oncology digital twins beyond hospital-based care. Continuous monitoring of heart rate, physical activity, respiratory function, sleep quality, oxygen saturation, and other physiological parameters generates digital biomarkers reflecting patient health status and treatment tolerance.[17]

Artificial intelligence integrates these real-time data with laboratory investigations, imaging findings, molecular biomarkers, and patient-reported outcomes to identify early signs of treatment toxicity, disease progression, or functional decline. Remote monitoring supports earlier clinical intervention, personalized follow-up, and improved survivorship care while reducing unnecessary hospital visits.[18]

17. Future Perspectives

The future of oncology digital twins will be shaped by continued advances in multimodal artificial intelligence, foundation models, generative AI, spatial biology, liquid biopsy, wearable technologies, quantum computing, and cloud-based healthcare infrastructure.[19]

Future digital twins are expected to function within intelligent oncology ecosystems that seamlessly integrate radiology, pathology, genomics, pharmacy systems, robotic surgery, adaptive radiation therapy, and electronic health records into continuously learning computational platforms. These systems will support predictive disease monitoring, adaptive treatment optimization, automated risk assessment, and increasingly personalized clinical care.[20]

Applications spanning cancer diagnosis, computational pathology, radiogenomics, immunotherapy, radiation oncology, surgical planning, drug discovery, and intelligent clinical decision support demonstrate the broad translational value of this technology. Nevertheless, successful implementation depends upon overcoming challenges related to interoperability, computational infrastructure, algorithmic bias, cybersecurity, regulatory validation, and clinician acceptance through multidisciplinary collaboration and rigorous prospective evaluation.[22]

longitudinal health data into unified computational models.[23]

Artificial intelligence enables these virtual patients to simulate disease progression, predict therapeutic response, optimize treatment planning, monitor toxicity, and support survivorship care throughout the cancer

journey. As advances in multimodal learning, explainable AI, foundation models, federated learning, and computational infrastructure continue to accelerate, digital twins are expected to become increasingly accurate, scalable, interpretable, and clinically applicable.[24]

Although important scientific, technical, ethical, and regulatory challenges remain, ongoing interdisciplinary research is steadily advancing digital twins toward

routine implementation in oncology practice. By enabling individualized simulation of disease evolution and therapeutic response, these technologies have the potential to transform cancer care from a predominantly reactive discipline into a predictive, adaptive, and highly personalized model of precision medicine, ultimately improving outcomes and quality of life for patients worldwide.[25]

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