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Review Article

Digital Twin Architectures for Personalized Cancer Imaging and Disease Progression Modeling

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Digital twin technology represents a paradigm shift in precision oncology, enabling the creation of dynamic, patient-specific virtual replicas that integrate multimodal imaging, molecular data, and clinical information to simulate disease progression and optimize personalized treatment strategies. Originally conceived in aerospace and manufacturing industries, digital twins – dynamic virtual replicas that evolve with real-time data inputs – are now poised to revolutionize cancer care by enabling truly personalized therapeutic strategies. Digital twins employ mathematical and computational models to virtually represent a physical object (e.g., planes and human organs), predict the behavior of the object, and enable decision-making to optimize the future behavior of the object. This comprehensive review synthesizes recent advances in digital twin architectures for oncology, emphasizing the integration of advanced medical imaging modalities, artificial intelligence and machine learning algorithms, radiomics analysis, and mechanistic disease progression models. The global digital twin market in healthcare is experiencing explosive growth, projected to reach USD 21.1 billion by 2028 with a compound annual growth rate exceeding 25%. Since 2020, research on digital twin technology in oncology has surged, with significant contributions from the United States, Germany, Switzerland, and China. Current applications span tumor segmentation, treatment response prediction, radiotherapy planning, immunotherapy optimization, and longitudinal disease monitoring. However, significant challenges remain in data standardization, model validation, regulatory frameworks, and clinical implementation. This review examines key architectural components of cancer digital twins, discusses successful applications across multiple cancer types, evaluates methodological approaches, identifies research gaps, and outlines future directions toward realizing the full clinical potential of this transformative technology for precision cancer medicine.

Keywords: digital twins, precision oncology, medical imaging, artificial intelligence, machine learning, radiomics, disease progression modeling, personalized medicine, computational biology, treatment response prediction.

INTRODUCTION

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. [1] Cancer remains a leading cause of global morbidity and mortality, with heterogeneous biological characteristics and variable treatment responses presenting substantial challenges to conventional population-based therapeutic approaches. Traditional cancer management relies heavily on static imaging assessments and population-averaged clinical guidelines, which fail to account for the dynamic nature of tumor biology and individual patient variability. A cancer patient digital twin integrates multiscale, multimodal patient data including genomics, proteomics, imaging, clinical records, and real-time monitoring to create a computational model that mirrors an individual patient's disease trajectory. [1] Unlike static predictive models, digital twins continuously assimilate new data, enabling dynamic adaptation as a patient's condition evolves. This real-time learning capability addresses a fundamental limitation of traditional clinical approaches, where treatment decisions are often based on population averages rather than individual characteristics. [1] While digital twins have been widely used in engineering for decades, their applications to oncology are only just emerging. Due to advances in experimental techniques quantitatively characterizing cancer, as well as advances in the mathematical and computational sciences, the notion of building and applying digital twins to understand tumor dynamics and personalize the care of cancer patients has been increasingly appreciated. [2] The convergence of multiple technological advances has created unprecedented opportunities for digital twin development in oncology. The increasing availability of biomedical data from large biobanks, electronic health records, medical imaging, wearable and ambient biosensors, and the lower cost of genome and microbiome sequencing have set the stage for the development of multimodal artificial intelligence solutions that capture the complexity of human health and disease. [4] In 2020, the US National Cancer Institute, and the US Department of Energy, through a trans-disciplinary research community at the intersection of advanced computing and cancer research, initiated team science collaborative projects to explore the development and implementation of predictive Cancer Patient Digital Twins. [5] Medical imaging plays a central role in contemporary oncology, providing non-invasive visualization of tumor anatomy, physiology, and molecular characteristics. Medical imaging is fundamental to digital twin technology, enabling patient-specific virtual models of anatomy and physiology. By integrating high-resolution modalities (Magnetic Resonance Imaging (MRI), Computed Tomography (CT), Positron Emission Tomography (PET), ultrasound) with computational frameworks, recent imaging advances now support real-time simulation, predictive modeling, and earlier disease detection. [6] Artificial intelligence and machine learning have dramatically enhanced the ability to extract actionable information from imaging data through automated segmentation, feature extraction, and prognostic modeling. The confluence of new technologies with artificial intelligence (AI) and machine learning (ML) analytical techniques is rapidly advancing the field of precision oncology, promising to improve diagnostic approaches and therapeutic strategies for patients with cancer. [7] Digital twins are virtual representations of health and disease processes that can integrate real-time data and simulations to predict, prevent, and personalize treatments. [8] Digital twin (DT) technology is revolutionizing clinical practice by integrating diverse epidemiological data sources to create dynamic, patient-specific simulations. By leveraging data from genomics, proteomics, imaging, sociodemographics, and real-world behaviors, DTs provide a computational framework to model disease progression, optimize treatments, and personalize health care interventions. [9] This review provides a comprehensive examination of digital twin architectures for personalized cancer imaging and disease progression modeling, integrating recent advances from 2020 to 2026 across imaging sciences, computational oncology, artificial intelligence, and precision medicine.

2. Concept and Architecture of Digital Twins in Oncology

A digital twin is a virtual model developed to accurately reflect a physical thing or a system. In radiology, a digital twin of a radiological device enables developers to test its characteristics, make alterations to the design or materials, and test the success or failure of the modifications in a virtual environment. [10] This work emphasizes that patient data, including images, are not operable (clinically), but that digital twins are. Based on the former, the latter can be created. Subsequently, virtual clinical operations can be performed towards selection of optimal therapies. [11] The architecture of a cancer digital twin comprises several integrated layers that work synergistically to enable personalized diagnosis, prognosis, and treatment planning. These digital replicas allow simulations of disease progression, optimize diagnostics, and personalize treatment plans based on individual genetic and lifestyle profiles. [12] A comprehensive digital twin framework for oncology integrates the following core components:

Patient Data Acquisition Layer: This foundation layer encompasses collection and harmonization of heterogeneous data from multiple sources. DTs represent virtual replicas that encapsulate both medical and physiological characteristics—such as tissues, organs, and biokinetic data—of patients. These virtual models facilitate a deeper understanding of disease progression and enhance the customization and optimization of treatment plans by modeling complex interactions between genetic factors and environmental influences. [13] Data sources include electronic health records containing demographic information, clinical parameters, and treatment history; medical imaging datasets from multiple modalities; genomic and transcriptomic data; proteomic signatures; and real-time monitoring data from wearable devices.

Imaging and Radiomics Layer: Radiomics is an emerging area in quantitative image analysis that aims to relate large-scale extracted imaging information to clinical and biological endpoints. The development of quantitative imaging methods along with machine learning has enabled the opportunity to move data science research towards translation for more personalized cancer treatments. [14] Accumulating evidence has indeed demonstrated that noninvasive advanced imaging analytics, that is, radiomics, can reveal key components of tumor phenotype for multiple three-dimensional lesions at multiple time points over and beyond the course of treatment. [14]

AI and Machine Learning Modeling Layer: This layer employs advanced computational algorithms to identify complex patterns within multidimensional data. Radiomics extracts numerous sub-visual quantitative features from medical images and converts them into mineable data. When combined with deep learning, a subset of AI capable of automatic hierarchical feature representation, these methods excel at identifying complex, nonlinear patterns within multiparametric MRI data that are imperceptible to the human eye or traditional models. [15]

Biological and Mechanistic Modeling Layer: Including mechanistic simulations that produce behavior based on explicitly defined biological hypotheses and multiscale mechanisms is beneficial. It enables the exploration of diverse therapeutic strategies and supports dynamic clinical decision-making through insights from network science, quantitative biology, and digital medicine. [16] Mathematical modeling has long been a cornerstone of radiotherapy for cancer, guiding treatment prescription, planning, and delivery through versatile applications. As we enter the era of medical big data, where the integration of molecular, imaging, and clinical data at both the tumor and patient levels could promise more precise and personalized cancer treatment, the role of mathematical modeling has become even more critical. [17]

Simulation and Prediction Layer: These virtual models can simulate disease progression, predict drug responses, and optimize treatment strategies before actual clinical implementation. [18] This comprehensive narrative review aims to summarize the main applications of mathematical modeling in radiotherapy, bridging the gap between classical models and the latest advancements. The review covers a wide range of applications, including radiobiology, clinical workflows, stereotactic radiosurgery/stereotactic body radiotherapy (SRS/SBRT), spatially fractionated radiotherapy (SFRT), FLASH radiotherapy (FLASH-RT), immune-radiotherapy, and the emerging concept of radiotherapy digital twins. [17]

Clinical Decision Support Layer: Multi-modal multi-scale images, combined with other data and aided by artificial intelligence (AI) techniques, will be utilized towards routine digital twinning of our patients, and will enable improved deliveries of RPTs and overall healthcare. [11] Digital twin technology is revolutionizing healthcare systems by leveraging real-time data integration, advanced analytics, and virtual simulations to enhance patient care, enable predictive analytics, optimize clinical operations, and facilitate training and simulation. [19]

These components interact synergistically to create a dynamic, adaptable system capable of evolving with patient data and clinical outcomes. DTs can use AI models to create predictions of future health outcomes for an individual patient in the form of an AI-generated digital twin to support the rapid assessment of in silico intervention strategies. DTs are gaining the ability to update in real time in relation to their corresponding physical patients and connect to multiple diagnostic and therapeutic devices. [20]

3. Role of Medical Imaging in Cancer Digital Twins

Medical imaging serves as the primary visual foundation for digital twin construction in oncology, providing anatomical, functional, and molecular information essential for comprehensive tumor characterization and disease monitoring. Such capabilities directly inform individualized treatment planning and contribute to more precise, personalized care. [6]

Multimodal Imaging Integration: Despite remaining challenges-complex anatomical modeling, multimodal integration, and high computational demands-recent advances in imaging and machine learning have significantly enhanced the accuracy and clinical utility of digital twins. [6] Different imaging modalities provide complementary information: The T1ce_FLAIR model, which integrates T1-contrast-enhanced (T1CE) and Fluid-Attenuated Inversion Recovery (FLAIR) sequences, achieved the highest Dice coefficients: 84.81% for peritumoral edema, 76.99% for enhancing tumors, and 72.25% for necrotic regions. [21]

Tumor Segmentation with Deep Learning: Automated tumor segmentation represents a critical preprocessing step enabling quantitative analysis and downstream prognostic modeling. Medical image segmentation is a critical component in clinical practice, facilitating accurate diagnosis, treatment planning, and disease monitoring. However, existing methods, often tailored to specific modalities or disease types, lack generalizability across the diverse spectrum of medical image segmentation tasks. [22] MedSAM, a foundation model designed for bridging this gap by enabling universal medical image segmentation, was developed on a large-scale medical image dataset with 1,570,263 image-mask pairs, covering 10 imaging modalities and over 30 cancer types. [22] The rapid development of artificial intelligence (AI) has gained importance, with many tools already entering our daily lives. The medical field of radiation oncology is also subject to this development, with AI entering all steps of the patient journey. [23] The integration of mathematical tumor growth models and AI-based tumor detection further enhances the possibilities for refining target volumes. [23]

Radiomics and Feature Extraction: These developments in the use of CT, PET, US, and MR imaging could augment patient stratification and prognostication buttressing emerging targeted therapeutic approaches. In recent years, deep learning architectures have demonstrated their tremendous potential for image segmentation, reconstruction, recognition, and classification. [14] Radiomics uses high-throughput data to extract various features from medical images with the potential to aid personalized precision medicine. Machine learning is a technique for analyzing and predicting by learning from sample data, finding patterns in it, and applying it to new data. [24]

AI-Based Image Analysis and Treatment Response Prediction: Deep learning techniques based on MRI have become valuable tools for predicting treatment responses in intestinal diseases, assisting clinicians in customizing personalized therapeutic strategies and improving patient outcomes. [15] Liu et al. introduced a deep-learning radiomics signature (DLRS) model based on multiparametric MRI to predict distant metastasis in patients with locally advanced rectal cancer following nCRT. The findings demonstrated that the DLRS could effectively stratify the risk of distant metastasis, with a 3-year AUC of 0.894 in the validation cohort. [15]

4. Artificial Intelligence and Machine Learning Integration

Advanced machine learning and deep learning architectures form the computational foundation enabling digital twins to identify complex patterns within high-dimensional, multimodal data and generate personalized predictions.

Deep Learning Architectures for Medical Imaging: This comprehensive review explores the role of deep learning (DL) in glioma segmentation using multiparametric magnetic resonance imaging (MRI) data. The study surveys advanced techniques such as multiparametric MRI for capturing the complex nature of gliomas. It delves into the integration of DL with MRI, focusing on convolutional neural networks (CNNs) and their remarkable capabilities in tumor segmentation. [25] We propose a novel cross-modal attention fusion-based deep neural network (CMAF-Net) for incomplete multimodal brain tumor segmentation, which is based on a three-dimensional (3D) U-Net architecture with encoding and decoding structure, a 3D Swin block, and a cross-modal attention fusion (CMAF) block. [26]

A 2.5D hybrid convolutional neural network was proposed to simultaneously localize glioma and classify its molecular status by leveraging MRI imaging features and prior knowledge features from clinical records and tumor location. [27] A brain tumor is an uncontrolled growth of cancerous cells in the brain. Accurate segmentation and classification of tumors are critical for subsequent prognosis and treatment planning. This work proposes context aware deep learning for brain tumor segmentation, subtype classification, and overall survival prediction using structural multimodal magnetic resonance images (mMRI). [28]

Multimodal Data Integration: By analyzing multi-dimensional, multiomic, spatial pathology, and radiomic data, these technologies enable a deeper understanding of the intricate molecular pathways, aiding in the identification of critical nodes within the tumor's biology to optimize treatment selection. [7] Digitized histopathological tissue slides and genomics profiling data are available for many patients with solid tumors. In the last 5 years, Deep Learning (DL) has been broadly used to extract clinically actionable information and biological knowledge from pathology slides and genomic data in cancer. In addition, a number of recent studies have introduced multimodal DL models designed to simultaneously process both images from pathology slides and genomic data as inputs. [29]

Explainable AI and Clinical Interpretability: Model transparency and explainability, achieved through techniques such as Grad-CAM (which generates visual heat maps highlighting regions that influence the model's decision), SHAP (a game-theoretic approach to quantify feature importance), and attention maps (from transformer models), are crucial for building clinician confidence and verifying that model decisions are based on clinically relevant imaging features. [15] Grad-CAM effectively identified regions that were significant for different tumour types, while SHAP analysis provided insights into the importance of individual features. Together, these approaches confirmed the reliability and interpretability of the model, overcoming key challenges in AI-driven medical diagnostics. [30]

Survival Prediction and Prognosis Modeling: Jiang et al. developed and validated a deep learning model utilizing a vision transformer (ViT) architecture to predict overall survival and disease-free survival in patients with rectal cancer using preoperative T2WI. The study included 893 patients from China and Germany, divided into training, validation, internal testing, and external testing cohorts. The model, trained on preoperative T2WI images, achieved a C-index of 0.82 for overall survival prediction in the validation set. [15]

5. Digital Twin Applications in Cancer Disease Progression Modeling

Successful digital twin implementations across multiple cancer types demonstrate the versatility and clinical potential of this approach, with emerging applications in diagnosis, treatment planning, response prediction, and longitudinal monitoring.

Brain Cancers and Glioblastoma: Glioblastoma presents an ideal clinical context for digital twin development due to its aggressive nature, complex heterogeneity, and limited therapeutic options. We previously demonstrated that the CUL2 gene, encoding the scaffold cullin2 protein in the cullin2-RING E3 ligase (CRL2), can predict GBM radiosensitivity and prognosis. CUL2 expression levels are closely regulated with its copy number variations (CNVs). This study aims to develop artificial neural networks (ANNs) for pretreatment evaluation of GBM patients with inputs obtainable without intracranial surgical biopsies. [31] The 4-layered deep learning ANN can identify a GBM patient's overall survival (OS) cohort with 80%–85% accuracy. The ANN requires 4 inputs, including CUL2 copy number, patients' age at GBM diagnosis, Karnofsky Performance Scale (KPS), and SvV ratio. [31] Using the BRIDGE co-registration workflow, a platform that integrates in vivo MRI with two-photon (2P) microscopy, in patient-derived glioblastoma models and human glioblastoma tissue, T2w signal intensities were correlated with tumor growth rates and density over time. [32] Mathematical modeling approaches have advanced treatment optimization: By accounting for the migration and infiltration of T cells within the tumor microenvironment, we established a quantitative link between radiation therapy and immunotherapy. Model parameters were estimated using a simulated annealing algorithm applied to training data, and our model achieved high accuracy for the test data with a root mean square error of 287 mm3. Notably, our framework replicated the PULSAR effect observed in animal studies, revealing that longer intervals between radiation treatments in the context of immunotherapy yielded enhanced tumor control. [33]

Lung Cancer: This study proposes a novel Smart Digital Twin Ecosystem (SDTE) that integrates RETFound with a multi-modal patient-specific digital twin to enable personalized diagnosis, real-time monitoring, and therapeutic planning for lung cancer. The architecture combines high-resolution thoracic CT scans, histopathology, genomic variants of EGFR, ALK, KRAS, and longitudinal clinical records to dynamically simulate tumor evolution and patient response. [34] RETFound was fine-tuned on an internal lung cancer dataset comprising 8,420 annotated CT studies from LIDC-IDRI and 2,135 histopathology samples from TCGA-LUAD and TCGA-LUSC. The proposed system achieved an average accuracy of 98.16%, Sensitivity of 97.92%, Specificity of 97.53%, Recall of 90.23% and F1-score 0.95. [34]

Breast Cancer: Breast cancer ranks as the second most concerning cause of death for women worldwide, with an expected 2.3 million new cases by 2024. The disease's development involves a mix of genetic mutations, hormonal elements, and environmental factors. [35] By amalgamating genetic, biochemical, and lifestyle data, digital twins could assist in safe diagnoses and tailor-made treatment plans. Progress in math, computer science, and experimental technology has propelled the usability of digital twins in cancer research areas, enhancing virtual experiments, treatment accessibility, and patient empowerment. [35]

Prostate Cancer: Digital twin (DT) technologies might represent an emerging conceptual framework aimed at supporting dynamic, patient-specific virtual modeling for personalized clinical decision-making. By integrating multimodal clinical, imaging, molecular, and physiological data, DTs can simulate disease progression, predict treatment responses, and support proactive, adaptive care. [36] Harnessing DTs could impact PCa management into a truly predictive, personalized, and participatory approach, improving outcomes and optimizing healthcare resource utilization globally. [36]

Colorectal Cancer: The adjuvant chemotherapy decision tree precisely identified patients likely to benefit from chemotherapy, reducing overtreatment by 65% and offering a clinically actionable tool for personalized therapeutic decision-making. [15] The joint analysis of pre-treatment and mid-treatment MRIs achieved an AUC of 0.83 in predicting pathological complete response. In a different study, Yi et al. created a machine-learning-based radiomics model using T2WI to evaluate tumor response to nCRT in patients with locally advanced rectal cancer, overcoming the limitations of traditional prediction methods. [15]

Mathematical Modeling of Tumor Growth and Treatment Response: AMBER is based on a voxelized geometry, enabling realistic simulations at relevant pre-clinical scales by tracking temporally discrete states stepwise. Its hybrid approach, combining traditional ABM techniques with continuous spatiotemporal fields of key microenvironmental factors such as oxygen and vascular endothelial growth factor, facilitates the generation of realistic tortuous vascular trees. [37] AMBER is integrated with TOPAS, an MC-based particle transport algorithm that simulates heterogeneous radiation doses. The impact of radiation on tumor dynamics considers the microenvironmental factors that alter radiosensitivity, such as oxygen availability, providing a full coupling between the biological and physical aspects. [37]

6. Personalized Cancer Treatment Using Digital Twins

Digital twins enable fundamentally new approaches to precision oncology by permitting in silico simulation of treatment responses before clinical administration, thereby optimizing therapeutic selection and reducing adverse effects.

Drug Response Prediction and Treatment Selection: In pharmacotherapy, digital twins combine mechanistic pharmacokinetic-pharmacodynamic modeling with artificial intelligence to simulate drug exposure and therapeutic response prior to treatment administration. This capability allows optimization of dosing, prediction of adverse drug reactions, and selection of individualized therapies. [38] Cancer heterogeneity presents a major obstacle to effective drug treatment, emphasizing the need for personalized approaches that can accurately predict drug responses. Advances in high-throughput technologies have driven precision medicine initiatives toward integrating multi-omics data, enabling a more comprehensive understanding of tumor biology. [39]

Patient-Derived Models and In Silico Trials: Computational models have been successful in predicting drug sensitivity in cancer cell line data, creating an opportunity to guide precision medicine. However, translating these models to tumors remains challenging. We propose a new transfer learning workflow that transfers drug sensitivity predicting models from large-scale cancer cell lines to both tumors and patient derived xenografts based on molecular pathways derived from genomic features. [40] We conducted this co-clinical trial with treatment-naive rectal cancer patients and matched patient-derived tumor organoids to determine whether a correlation exists between experimental results obtained after irradiation in patients and organoids. [41] Our machine learning-based prediction model showed excellent performance. In the prediction model for good responders trained using the random forest algorithm, the area under the curve, accuracy, and kappa value were 0.918, 81.5%, and 0.51, respectively. In the prediction model for poor responders, the area under the curve, accuracy, and kappa value were 0.971, 92.1%, and 0.75, respectively. [41]

Radiotherapy Planning and Optimization: We evaluate the mathematical implications and biological effects of 2 models of RT response on dose personalization: (1) cytotoxicity to cancer cells that lead to direct tumor volume reduction (DVR) and (2) radiation responses to the tumor microenvironment that lead to tumor carrying capacity reduction (CCR) and subsequent tumor shrinkage. [42] Since CT scans form an integral part of radiotherapy, a widely used cancer treatment, we propose the use of CT-derived radiomic features to attempt to predict the course of tumor growth curves. [43]

Immunotherapy and Combination Treatment Optimization: Drug resistance is one of the most intractable issues to the targeted therapy for cancer diseases. To explore effective combination therapy schemes, we propose a mathematical model to study the effects of different treatment schemes on the dynamics of cancer cells. [44] Simulation results suggest that immunotherapy combined with chemotherapy contributes significantly to the control of tumor growth compared to monotherapy. [44] We present a novel macroscopic approach designed to quantitatively analyze the intricate dynamics governing the interactions among the immune system, radiotherapy, and tumor progression. Building upon previous research demonstrating the synergistic effects of radiotherapy and immunotherapy in cancer treatment, we provide a comprehensive mathematical framework for understanding the underlying mechanisms driving these interactions. [45]

7. Current Challenges and Limitations

Despite tremendous progress, significant obstacles impede widespread clinical implementation of cancer digital twins, necessitating continued research and infrastructure development.

Data Quality, Standardization, and Interoperability: On the application of data processing and artificial intelligence, the algorithm for combining medical imaging and multi-omics data is the key, and the integration of multi-modal data and dynamic modeling improve the accuracy of the model, but the integration of different data types is limited by the interoperability of the tools and the degree of standardization. [3] Data integration across heterogeneous sources presents substantial technical hurdles, requiring robust frameworks for harmonizing genomic, imaging, and clinical data under findability, accessibility, interoperability, reusability principles. [1]

Model Validation and Clinical Evidence: Importantly, most published work emphasizes technical accuracy, with limited evidence demonstrating that AI-assisted MRI prognostication improves patient outcomes, clinical decision-making, or cost-effectiveness—underscoring a significant translational gap. [15] Several challenges hinder the broader implementation of MDT, including the integration of heterogeneous data sources, interpretability and generalizability of artificial intelligence models, data security and privacy concerns, and the need for scalable computational infrastructures. [46]

Computational Complexity and Infrastructure Requirements: The complexity of cancer biology – including mechanisms of drug resistance, immune responses, and inter-patient heterogeneity – poses challenges for mechanistic modeling, particularly in immuno-oncology, where treatment mechanisms are not fully understood. [1] Widespread implementation faces several challenges: (1) characterizing dynamic molecular changes across multiple biological scales; (2) developing computational methods to integrate data into DTs; (3) prioritizing disease mechanisms and therapeutic targets; (4) creating interoperable DT systems that can learn from each other; (5) designing user-friendly interfaces for patients and clinicians; (6) scaling DT technology globally for equitable healthcare access; (7) addressing ethical, regulatory, and financial considerations. [8]

Regulatory and Ethical Considerations: Regulatory frameworks remain underdeveloped. Bodies, including the Food and Drug Administration and European Medicines Agency will need to establish clear guidelines for validating and deploying digital twins in clinical settings, similar to existing frameworks for medical devices. [1] Furthermore, ethical considerations regarding data privacy, algorithmic bias, and equitable access needs careful attention to ensure this technology benefits all patients. [1]

Clinical Implementation and Workflow Integration: To become a standard of care, these models must demonstrate efficacy and safety through prospective trials, ultimately seeking approval as a software as a medical device (SaMD), a paradigm now being operationalized in pioneering clinical trials. [18] Yet, their routine application in clinical practice remains limited, underscoring a growing translational gap between digital innovation and healthcare delivery. [47]

FUTURE PERSPECTIVES

Emerging technological advances and evolving clinical needs point toward a future where digital twins become foundational elements of precision cancer medicine, with several promising directions warranting investigation.

Real-Time Monitoring and Adaptive Treatment: For real-time monitoring and adaptation, digital twins continuously integrate data from clinical encounters, imaging, and even wearable devices to track disease progression and treatment response. This enables clinicians to adjust protocols dynamically – critical in oncology where tumor biology and treatment responsiveness vary significantly over time and between individuals. [1] Predictive analytics and preventive interventions are made possible by machine learning algorithms, allowing for early detection of health risks and proactive interventions. [19]

AI-Powered Autonomous Clinical Decision Systems: In clinical trial design, digital twins enable in silico simulation of trial outcomes, optimizing study designs and accelerating drug development. Virtual patient populations can be generated to test hypotheses, identify potential biomarkers for patient stratification, and predict treatment responses before human exposure – potentially reducing the time and cost associated with traditional clinical trials. [1] Generative AI has the potential to transform the field by leveraging recent developments in deep learning and customizing models for the needs of scientists, physicians and patients. [48]

Multi-Scale and Multi-Organ Modeling: Future research and development opportunities in healthcare span multiple scales, from molecular mechanisms to tissue-scale processes to whole-organism physiology, requiring integration across these biological levels. [4] The massive amount of human biological, imaging, and clinical data produced by multiple and diverse sources necessitates integrative modeling approaches able to summarize all this information into answers to specific clinical questions. [49]

Integration of Genomics and Spatial Omics: Spatial omics technologies correlate molecular signatures within tumor microenvironments, guiding treatment strategies. Bioinformatics integrates these technologies to establish a new standard in precision oncology, thereby enhancing therapy efficacy. [50] Multiomics data integration approaches offer a comprehensive functional understanding of biological systems, with significant applications in disease therapeutics. By providing deep insights into disease-associated molecular mechanisms, multiomics facilitates precision medicine by accounting for individual omics profiles, enabling early disease detection and prevention, aiding biomarker discovery for diagnosis, prognosis, and treatment monitoring, and identifying molecular targets for innovative drug development or the repurposing of existing therapies. [51]

Patient-Centered Design and Equitable Implementation: Future healthcare and public health policy must go beyond technical innovation to address patients' lived experiences, ensuring that digital twins enhance rather than diminish autonomy, trust, and equity. [52] We outline a translational roadmap that emphasizes dynamic model validation, clinician co-development, equitable data representation, and regulatory harmonization. [47]

CONCLUSION

Digital twin technology represents a transformative paradigm shift in oncology, moving cancer care from population-based medicine toward truly individualized, dynamic, predictive therapeutic strategies. Digital twins represent more than incremental technological advancement – they embody a fundamental reconceptualization of cancer care from population-based medicine to truly individualized therapy. [1] In this review, we present the opportunities and challenges of applying digital twins in clinical oncology, with a particular focus on integrating medical imaging with mechanism-based, tissue-scale mathematical modeling. [2] The successful integration of advanced medical imaging, machine learning algorithms, radiomics analysis, and mechanistic disease progression models has demonstrated the feasibility and clinical utility of digital twins across multiple cancer types, including glioblastoma, lung cancer, breast cancer, prostate cancer, and colorectal cancer. Digital twin technology has obvious advantages in diagnosis, treatment decision-making, prognosis prediction, and surgery planning. [3] AI-generated DTs now offer the potential to accurately diagnose cancer, reveal novel biomarkers, and accelerate drug development, thus advancing precision medicine. [7] However, widespread clinical adoption remains limited by challenges in data standardization, model validation, regulatory frameworks, and infrastructure requirements. The effective development and implementation of medical digital twins require a systems-based approach that extends beyond technological advancement to include integrated data infrastructures, interoperability standards, and robust data governance frameworks. Strengthening interdisciplinary collaboration among clinicians, data scientists, engineers, and policymakers is essential for ensuring the safe and effective use of this technology. [46] Future advancement requires sustained collaborative effort across computational, experimental, and clinical communities. With advancements in AI, wearable technology, and multiomics data integration, DTs are poised to reshape precision medicine. Future research should focus on refining computational efficiency, standardizing data interoperability, and ensuring ethical AI-driven decision-making. [9] The convergence of artificial intelligence, mathematical modeling, and clinical oncology in digital twin technology offers hope for a future where virtual experiments on patient-specific models may guide clinical decisions with unprecedented precision. The convergence of artificial intelligence, mathematical modeling, and clinical oncology in digital twin technology offers hope for a future where virtual experiments on patient-specific models may guide clinical decisions with unprecedented precision. [1] As computational capabilities expand, data integration improves, and validation studies accumulate, digital twins are poised to become foundational elements of next-generation precision oncology, ultimately enabling each cancer patient to receive care optimized specifically for their unique disease biology and individual characteristics.

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