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INTELLIGENT DIGITAL TWINS IN ONCOLOGY: REAL-TIME VIRTUAL PATIENT MODELING FOR PERSONALIZED THERAPEUTIC DECISION-MAKING

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Abstract: Digital twin technology is emerging as one of the most transformative innovations in precision oncology by enabling the creation of continuously evolving virtual representations of individual cancer patients capable of supporting real-time therapeutic decision-making. Conventional oncology frequently relies on episodic clinical assessments and fragmented diagnostic information that inadequately capture the dynamic biological evolution of tumors throughout diagnosis, treatment, recurrence, metastasis, and survivorship. Recent advances in artificial intelligence (AI), foundation models, multimodal transformer architectures, graph neural networks, self-supervised learning, and generative AI have enabled integration of radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, electronic health records, and longitudinal clinical outcomes into adaptive virtual patient models. These intelligent digital twins continuously synchronize with evolving patient biology, supporting precision diagnosis, biomarker discovery, prognostic prediction, therapeutic optimization, immunotherapy selection, toxicity prediction, adaptive disease monitoring, and personalized clinical decision support. Emerging technologies including multimodal large language models, federated learning, reinforcement learning, retrieval-augmented generation, explainable artificial intelligence, and agentic AI further enhance digital twin ecosystems by enabling collaborative, privacy-preserving, transparent, and continuously adaptive computational intelligence. Despite remarkable technological progress, significant scientific, technical, ethical, and regulatory challenges remain regarding multimodal data harmonization, computational scalability, interoperability, explainability, cybersecurity, clinical validation, and equitable implementation. This review provides a comprehensive overview of intelligent digital twins in oncology, emphasizing real-time virtual patient modeling for personalized therapeutic decision-making as a transformative paradigm for next-generation precision cancer care.[1]

Keywords: *Digital twins, Precision oncology, Artificial intelligence, Foundation models, Virtual patients, Computational oncology, Personalized medicine, Clinical intelligence, Multi-omics, Clinical decision support.*

1. Introduction

Cancer is a highly dynamic biological disease characterized by continuous genomic evolution, epigenetic remodeling, immune adaptation, metabolic reprogramming, angiogenesis, tissue remodeling, and complex interactions among malignant cells, stromal components, immune populations, and host physiology. These biological processes continuously evolve throughout diagnosis, treatment, recurrence, metastasis, and survivorship, making precision oncology increasingly dependent upon computational systems capable of continuously integrating heterogeneous biomedical information.[2]

Modern oncology generates enormous quantities of biomedical data through radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, circulating tumor DNA, wearable physiological monitoring, physician

documentation, electronic health records, and patient-reported outcomes. Although each modality contributes unique biological insight, isolated interpretation frequently fails to capture the systems-level interactions governing tumor evolution, therapeutic response, resistance mechanisms, and long-term clinical outcomes.[3]
Digital twin technology has emerged as a transformative computational paradigm by creating continuously evolving virtual representations of individual patients capable of integrating multimodal biomedical intelligence into predictive computational simulations. Combined with foundation AI models, digital twins provide unprecedented opportunities for personalized therapeutic planning, adaptive disease monitoring, and real-time precision oncology.
The convergence of artificial intelligence and digital twins therefore establishes the foundation for intelligent virtual patient ecosystems capable of transforming future cancer care.[4]

2. Evolution of Digital Twin Technology in Oncology

Digital twin technology originated in engineering as a computational methodology for continuously synchronizing virtual models with physical systems through real-time data integration. Advances in artificial intelligence, cloud computing, biomedical informatics, and computational biology have enabled translation of this concept into healthcare, where digital twins increasingly represent individual patients rather than mechanical systems.[5]
Early oncology applications primarily focused on mathematical simulation of tumor growth and treatment response. Subsequent integration of radiological imaging, computational pathology, genomics, laboratory biomarkers, and electronic health records expanded digital twin capabilities toward comprehensive patient modeling.
More recently, foundation AI models, multimodal learning, reinforcement learning, federated learning, graph neural networks, and multimodal large language models have transformed digital twins into intelligent computational ecosystems capable of continuously learning from evolving biomedical evidence while supporting adaptive precision medicine.[6]

3. Principles of Intelligent Digital Twins

Intelligent digital twins differ fundamentally from conventional predictive models because they continuously synchronize with evolving patient biology throughout diagnosis, treatment, recurrence, and survivorship. Foundation AI models integrate radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, wearable physiological monitoring, physician documentation, patient-reported outcomes, and longitudinal clinical trajectories into unified patient-specific computational representations.[7]
Self-supervised learning enables discovery of latent biological relationships without requiring extensive manual annotation, while multimodal transformer architectures align heterogeneous biomedical modalities within shared computational embedding spaces. Graph neural networks further characterize interactions among genes, proteins, signaling pathways, immune populations, imaging phenotypes, tissue architecture, therapeutic targets, physiological variables, and clinical outcomes.
These computational principles establish continuously adaptive virtual patients capable of supporting predictive precision oncology throughout the cancer care continuum.[8]

4. Computational Architecture of Oncology Digital Twins

Modern oncology digital twin platforms consist of interconnected computational layers responsible for multimodal biomedical data acquisition, preprocessing, representation learning, multimodal fusion, predictive simulation, adaptive learning, virtual patient synchronization, and intelligent clinical decision support.[9]
The acquisition layer continuously integrates radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, circulating tumor DNA, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and electronic health records.

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Advanced preprocessing pipelines normalize imaging studies, harmonize molecular datasets, encode clinical narratives using natural language processing, and synchronize temporal patient information.

Foundation AI models subsequently generate generalized multimodal embeddings representing molecular biology, tissue architecture, imaging phenotypes, physiological function, and longitudinal clinical trajectories. These adaptive computational representations continuously evolve alongside biological patient changes while supporting predictive simulation and therapeutic optimization.[10]

5. Foundation AI Models as the Intelligence Engine

Foundation AI models represent the computational intelligence underlying digital twin ecosystems because they acquire generalized biomedical knowledge from massive multimodal datasets before adaptation to specialized oncology applications. Unlike conventional task-specific algorithms, foundation models develop transferable computational representations applicable across diagnosis, prognosis, biomarker discovery, therapeutic prediction, disease monitoring, radiomics, computational pathology, immunotherapy, and intelligent clinical decision support.[11]

Transformer architectures enable multimodal attention across imaging, pathology, molecular biology, laboratory investigations, wearable monitoring, and clinical documentation, while graph neural networks characterize interactions among signaling pathways, immune responses, imaging phenotypes, therapeutic targets, physiological variables, and longitudinal clinical outcomes.

These generalized computational capabilities establish foundation AI models as continuously evolving biomedical reasoning engines supporting intelligent digital twins throughout precision oncology.[12]

6. Multimodal Biomedical Integration

Comprehensive virtual patient modeling requires seamless integration of complementary biomedical modalities into unified patient-specific computational representations. Radiological imaging provides anatomical and functional characterization of tumors, digital pathology reveals microscopic tissue architecture, and multi-omics technologies—including genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, microbiomics, and spatial biology—provide comprehensive molecular characterization of evolving cancer biology.[13]

Wearable biosensors continuously monitor physiological parameters including heart rate, sleep quality, physical activity, treatment-related symptoms, medication adherence, and quality-of-life indicators, while electronic health records contribute longitudinal clinical context extending beyond conventional hospital-based assessments.

Artificial intelligence harmonizes these diverse biomedical modalities using multimodal transformers, graph neural networks, biological knowledge graphs, and cross-modal attention mechanisms capable of generating adaptive computational embeddings representing continuously evolving patient biology.[14]

7. Real-Time Virtual Patient Modeling

The defining characteristic of intelligent oncology digital twins is continuous synchronization between biological patients and their computational counterparts. Foundation AI models continuously analyze serial radiological imaging, digital pathology, circulating tumor DNA, laboratory biomarkers, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and longitudinal clinical trajectories while updating virtual patient representations in real time.[15]

Unlike static predictive models, digital twins dynamically adapt to evolving tumor biology, therapeutic response, physiological changes, emerging biomarkers, treatment-related toxicity, and disease progression. These adaptive capabilities enable continuous monitoring of disease evolution while supporting individualized therapeutic planning based on current patient status rather than historical information.

Real-time virtual patient modeling therefore establishes digital twins as continuously evolving

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computational companions throughout cancer management.[16]

8. Predictive Simulation and Therapeutic Optimization

Intelligent digital twins enable predictive simulation of alternative therapeutic strategies before clinical implementation. Foundation AI models integrate molecular biology, imaging phenotypes, tissue architecture, laboratory biomarkers, physiological monitoring, and longitudinal clinical trajectories to simulate responsiveness to chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment combinations.[17]

Virtual simulations estimate treatment efficacy, toxicity, recurrence probability, progression-free survival, overall survival, quality of life, and mechanisms of therapeutic resistance while continuously refining predictive accuracy as additional biomedical information becomes available.

These computational simulations support personalized therapeutic optimization by identifying treatment strategies most likely to maximize clinical benefit while minimizing adverse effects.[18]

9. Personalized Clinical Decision-Making

One of the most clinically significant applications of intelligent oncology digital twins is personalized therapeutic decision-making through continuous integration of multimodal biomedical intelligence. Digital twins simultaneously analyze molecular alterations, imaging phenotypes, histopathological characteristics, physiological monitoring, laboratory biomarkers, medication history, and longitudinal clinical trajectories to generate individualized therapeutic recommendations while continuously adapting these recommendations according to evolving patient biology, treatment response, and real-world clinical outcomes. This adaptive computational framework establishes intelligent virtual patients as powerful decision-support systems capable of enhancing multidisciplinary precision oncology throughout the entire cancer care continuum.[19][20]

10. Intelligent Clinical Decision Support Through Digital Twins

Intelligent digital twins provide the computational infrastructure for next-generation clinical decision-support systems capable of integrating heterogeneous biomedical information into comprehensive patient-centered recommendations. Rather than interpreting radiological imaging, digital pathology, molecular diagnostics, laboratory investigations, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and evidence-based clinical guidelines independently, digital twin ecosystems synthesize these diverse biomedical data into unified computational representations supporting multidisciplinary oncology practice.[21]

Interactive clinical dashboards generate individualized diagnostic summaries, multimodal biomarker analyses, virtual therapeutic simulations, toxicity estimates, recurrence probabilities, disease progression forecasts, and survival predictions while facilitating collaboration among oncologists, radiologists, pathologists, surgeons, radiation oncologists, molecular biologists, pharmacists, nurses, genetic counselors, and computational scientists. These intelligent systems improve workflow efficiency, strengthen multidisciplinary communication, reduce information fragmentation, and promote evidence-based personalized cancer management throughout the cancer care continuum.

11. Continuous Learning and Adaptive Virtual Patients

A defining characteristic of intelligent oncology digital twins is their ability to continuously evolve as new biomedical information becomes available. Artificial intelligence incorporates serial imaging examinations, computational pathology, circulating tumor DNA, laboratory biomarkers, wearable physiological monitoring, medication adherence, physician documentation, patient-reported outcomes, and real-world clinical evidence into adaptive computational frameworks capable of continuously refining predictive accuracy throughout the patient's clinical journey.[22]

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Continual learning algorithms enable incremental refinement of computational knowledge without catastrophic forgetting of previously acquired information, while reinforcement learning optimizes therapeutic recommendations through iterative evaluation of treatment outcomes. As a result, digital twins remain synchronized with evolving tumor biology, emerging scientific discoveries, changing clinical guidelines, and individualized patient trajectories.

This adaptive computational paradigm transforms virtual patient modeling into a continuously learning system capable of supporting real-time precision oncology.

12. Digital Twins for Precision Immunotherapy and Combination Treatment

The complexity of tumor–immune interactions makes immunotherapy particularly well suited for digital twin–based computational modeling. Intelligent virtual patients integrate computational pathology, radiomics, immunomics, genomics, transcriptomics, proteomics, spatial biology, circulating tumor DNA, laboratory biomarkers, and longitudinal clinical outcomes into comprehensive simulations of tumor–immune ecosystem dynamics.[23]

Foundation AI models predict responsiveness to immune checkpoint inhibitors, adoptive cellular therapies, cancer vaccines, bispecific antibodies, cytokine-based therapies, and multimodal combination regimens while simultaneously estimating immune-related adverse events and mechanisms of therapeutic resistance.

Digital twin simulations therefore enable individualized optimization of combination therapies by evaluating alternative treatment strategies before clinical implementation, thereby improving therapeutic precision while minimizing unnecessary toxicity.

13. Federated Digital Twin Ecosystems

Development of highly accurate and generalizable digital twin platforms requires access to diverse biomedical datasets representing multiple healthcare systems, imaging technologies, molecular profiling platforms, treatment protocols, and patient populations. Federated learning enables collaborative development of intelligent digital twins while preserving patient privacy and institutional governance through decentralized computational training.[24]

Participating healthcare institutions independently train local digital twin models using radiological imaging, digital pathology, genomics, laboratory investigations, wearable monitoring, liquid biopsy, and longitudinal clinical records while securely exchanging encrypted model parameters instead of identifiable patient information. This collaborative learning strategy substantially improves algorithm robustness, fairness, external validity, and clinical generalizability across diverse healthcare environments.

Federated digital twin ecosystems therefore establish international computational oncology networks capable of accelerating scientific discovery while maintaining responsible biomedical data stewardship.

14. Explainability, Validation, and Ethical Governance

Successful implementation of intelligent digital twins requires transparent, interpretable, reproducible, and rigorously validated computational systems capable of supporting clinician confidence, patient trust, and regulatory approval. Explainable artificial intelligence (XAI) enables clinicians to understand digital twin reasoning through attention visualization, saliency maps, SHAP (Shapley Additive Explanations), feature attribution analysis, uncertainty estimation, and counterfactual explanations identifying the imaging, molecular, pathological, physiological, and clinical variables contributing to computational predictions.[25]

Clinical deployment additionally requires standardized multimodal datasets, interoperable computational infrastructure, prospective multicenter validation, external benchmarking, cybersecurity safeguards, continuous monitoring for algorithmic bias, and compliance with evolving international regulatory frameworks governing AI-enabled healthcare technologies.

Responsible implementation further depends upon patient privacy, informed consent, transparency, accountability, equitable access, responsible data governance, and continuous post-deployment surveillance to ensure trustworthy integration of digital twin technology into routine oncology practice.

15. Future Perspectives

Future intelligent digital twin ecosystems will increasingly integrate multimodal foundation models, multimodal large language models, agentic artificial intelligence, graph neural networks, reinforcement learning, federated learning, spatial multi-omics, liquid biopsy, quantum computing, Internet of Medical Things (IoMT), robotics, cloud-native healthcare infrastructure, and autonomous clinical reasoning systems into comprehensive precision oncology platforms.[26]

These next-generation computational ecosystems will continuously integrate molecular biology, radiological imaging, digital pathology, laboratory medicine, wearable physiological monitoring, environmental exposures, electronic health records, biomedical literature, and real-world clinical outcomes while autonomously coordinating diagnostic workflows, optimizing therapeutic strategies, supporting adaptive clinical trials, generating personalized patient communication, and continuously synthesizing biomedical evidence.

Such intelligent digital twins are expected to transform oncology from fragmented and reactive disease management toward predictive, preventive, adaptive, and continuously learning precision healthcare.

16. Discussion

Intelligent digital twins represent one of the most significant paradigm shifts in computational oncology by integrating multimodal biomedical intelligence into continuously evolving virtual patient ecosystems capable of supporting comprehensive personalized cancer care. Unlike conventional predictive algorithms developed for isolated clinical tasks, digital twins simultaneously analyze molecular biology, tissue architecture, radiological imaging, laboratory biomarkers, physiological monitoring, environmental influences, and longitudinal clinical trajectories to generate holistic computational representations of evolving cancer biology.[27]

Applications spanning computational pathology, radiogenomics, biomarker discovery, precision immunotherapy, adaptive therapeutics, disease surveillance, survivorship management, clinical trial optimization, continuous learning, and intelligent clinical decision support demonstrate the extraordinary potential of digital twin technology to redefine future oncology. Nevertheless, successful implementation requires continued advances in multimodal data harmonization, explainable artificial intelligence, interoperability, computational infrastructure, cybersecurity, regulatory science, ethical governance, and sustained multidisciplinary collaboration.

As biomedical knowledge and healthcare data continue to expand exponentially, intelligent digital twins are expected to become one of the foundational computational infrastructures supporting precision oncology worldwide.

17. Conclusion

Intelligent digital twins are transforming precision oncology by integrating radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable technologies, electronic health records, foundation AI models, and longitudinal clinical intelligence into unified virtual patient ecosystems capable of supporting accurate diagnosis, biomarker discovery, prognostic prediction, therapeutic optimization, adaptive disease monitoring, and personalized therapeutic decision-making throughout the cancer care continuum.[28]

Advances in transformer architectures, multimodal learning, graph neural networks, self-supervised learning, federated learning, reinforcement learning, multimodal large language models, agentic AI, and generative artificial intelligence are expected to further strengthen digital twin ecosystems, enabling increasingly accurate molecular characterization, predictive clinical intelligence, adaptive therapeutics, continuous disease surveillance, and individualized oncology care.[29]

Although important scientific, technical, ethical, regulatory, and implementation challenges

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remain, sustained collaboration among oncologists, radiologists, pathologists, molecular biologists, biomedical engineers, computer scientists, healthcare organizations, policymakers, industry partners, and regulatory agencies will accelerate the responsible implementation of intelligent digital twins in oncology. These innovations have the potential to improve patient outcomes, enhance healthcare efficiency, reduce disparities in cancer care, accelerate translational research, and establish a new era of intelligent, adaptive, and continuously learning precision cancer medicine worldwide.[30]

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