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DIGITAL TWIN–ENABLED PRECISION ONCOLOGY: INTEGRATING LONGITUDINAL PATIENT DATA, MULTI-OMICS, AND ARTIFICIAL INTELLIGENCE

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Abstract: Digital twin technology is rapidly emerging as one of the most transformative innovations in precision oncology by enabling continuously evolving virtual representations of individual cancer patients capable of supporting predictive, personalized, and adaptive clinical decision-making. Traditional oncology frequently depends on fragmented interpretation of radiological imaging, molecular diagnostics, pathological findings, and episodic clinical assessments, limiting comprehensive understanding of the dynamic biological evolution of cancer. Recent advances in artificial intelligence (AI), foundation models, multimodal transformer architectures, graph neural networks, self-supervised learning, and generative AI have enabled seamless integration of longitudinal patient data, radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, electronic health records, and real-world clinical outcomes into adaptive virtual patient ecosystems. These intelligent digital twins continuously synchronize with evolving patient biology to support 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 strengthen digital twin ecosystems by enabling collaborative, privacy-preserving, transparent, and continuously adaptive computational intelligence. Despite remarkable technological progress, important 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 digital twin–enabled precision oncology, emphasizing integration of longitudinal patient data, multi-omics, and artificial intelligence as a transformative framework for next-generation personalized cancer medicine.[1]
Keywords: *Digital twins, Precision oncology, Artificial intelligence, Longitudinal patient data, Multi-omics, Foundation models, Computational oncology, Personalized medicine, Clinical intelligence, Virtual patients.*

1. Introduction

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

Modern oncology generates enormous quantities of biomedical information 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 valuable biological insight, isolated interpretation frequently overlooks systems-level relationships governing disease progression, 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 and longitudinal patient monitoring, digital twins provide unprecedented opportunities for personalized therapeutic planning, adaptive disease monitoring, and real-time precision oncology.
The convergence of artificial intelligence, longitudinal biomedical data, and digital twins therefore establishes the foundation for intelligent virtual patient ecosystems capable of transforming future cancer care.[4]

2. Evolution of Digital Twins in Precision Oncology

Digital twin technology originated in engineering as a computational methodology for continuously synchronizing virtual models with physical systems through real-time sensor integration. Advances in artificial intelligence, cloud computing, computational biology, and biomedical informatics have enabled translation of this concept into healthcare, where digital twins increasingly represent individual patients rather than mechanical systems.[5]
Initial oncology applications primarily focused on mathematical simulation of tumor growth and therapeutic response. Subsequent integration of radiological imaging, computational pathology, genomic profiling, 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, multimodal large language models, and agentic AI 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 Oncology 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, circulating tumor DNA, 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

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. Advanced preprocessing pipelines normalize imaging studies, harmonize molecular datasets, encode clinical narratives using natural language processing, synchronize temporal patient information, and integrate longitudinal observations collected throughout the patient's disease course.

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 evolve continuously alongside biological patient changes while supporting predictive simulation and therapeutic optimization.[10]

5. Longitudinal Patient Data as the Foundation of Digital Twins

Longitudinal patient data represent the defining characteristic of intelligent digital twin ecosystems because they enable continuous synchronization between biological patients and their computational counterparts. Serial radiological imaging, repeated molecular profiling, laboratory investigations, wearable physiological monitoring, medication adherence records, physician documentation, patient-reported outcomes, and survivorship data collectively describe the dynamic evolution of cancer throughout diagnosis, treatment, recurrence, metastasis, and long-term follow-up.[11]

Foundation AI models analyze these temporal datasets using recurrent transformers, temporal graph neural networks, sequential attention mechanisms, and continual learning algorithms capable of recognizing evolving disease trajectories rather than isolated clinical events. Consequently, longitudinal computational representations substantially improve prediction of therapeutic response, recurrence, toxicity, disease progression, and survival while supporting adaptive clinical decision-making.

These continuously updated patient histories transform digital twins into living computational representations that evolve alongside real patients.[12]

6. Multi-Omics Integration

Comprehensive molecular characterization represents one of the greatest strengths of digital twin–enabled precision oncology. Artificial intelligence integrates genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, microbiomics, spatial biology, and single-cell sequencing into generalized molecular representations capable of characterizing evolving tumor biology across multiple organizational scales.[13]

Transformer architectures identify latent biological relationships among genes, proteins, signaling pathways, metabolites, immune responses, and therapeutic targets, while graph neural networks model complex biological interaction networks supporting systems-level computational reasoning.

These integrated molecular representations substantially improve biomarker discovery, molecular subtype classification, therapeutic response prediction, systems biology research, and individualized precision medicine while continuously updating virtual patient biology.[14]

7. Imaging Intelligence and Digital Pathology

Radiological imaging and digital pathology provide complementary information describing cancer biology across macroscopic and microscopic organizational scales. Foundation AI models automatically extract generalized imaging and pathomic representations from computed tomography, magnetic resonance imaging, positron emission tomography, ultrasound, and whole-slide pathology images without requiring handcrafted feature engineering.[15]

Artificial intelligence identifies latent imaging biomarkers associated with molecular alterations, immune infiltration, angiogenesis, fibrosis, hypoxia, therapeutic responsiveness, treatment resistance, and disease progression. Integration of imaging intelligence with longitudinal molecular

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biology substantially improves diagnosis, prognostic prediction, biomarker discovery, therapeutic optimization, and adaptive disease monitoring.

These imaging representations provide continuously updated non-invasive computational windows into evolving tumor biology.[16]

8. Artificial Intelligence for Adaptive Virtual Patient Modeling

Artificial intelligence functions as the computational intelligence underlying digital twin ecosystems by continuously integrating longitudinal patient information with multimodal biomedical data. Foundation AI models employ multimodal transformers, graph neural networks, reinforcement learning, and continual learning algorithms to synchronize virtual patients with evolving biological counterparts while refining predictive accuracy as new clinical evidence becomes available.[17]

Adaptive virtual patient modeling enables simulation of disease progression, therapeutic response, treatment-related toxicity, recurrence, metastatic dissemination, and survivorship outcomes under alternative clinical scenarios. This continuous computational adaptation allows digital twins to evolve throughout the patient's clinical journey while supporting increasingly personalized oncology care.[18]

9. Personalized Therapeutic Decision-Making

One of the most clinically important applications of digital twin–enabled precision oncology is individualized therapeutic optimization through comprehensive integration of longitudinal patient data, molecular biology, imaging phenotypes, histopathological characteristics, laboratory biomarkers, wearable physiological monitoring, medication history, and longitudinal clinical trajectories. Foundation AI models continuously predict responsiveness to chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment combinations while adapting therapeutic recommendations according to evolving patient biology, treatment response, toxicity profiles, and real-world clinical outcomes. These adaptive computational systems establish intelligent virtual patients capable of supporting predictive, personalized, and continuously optimized cancer treatment throughout the disease continuum.[19][20]

10. Intelligent Clinical Decision Support

Digital twin–enabled precision oncology provides 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 information sources 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 fragmentation of biomedical information, 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

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evidence into adaptive computational frameworks capable of continuously refining predictive accuracy throughout the patient's clinical journey.[22]

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. Consequently, 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 Therapy

The complexity of tumor–immune interactions makes immunotherapy particularly suitable 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, electronic health records, and longitudinal clinical records while securely exchanging encrypted model parameters rather than 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 digital twin–enabled precision oncology 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

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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 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

Digital twin–enabled precision oncology represents one of the most significant paradigm shifts in computational oncology by integrating longitudinal patient data, multi-omics, artificial intelligence, radiological imaging, digital pathology, laboratory biomarkers, and clinical 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, imaging phenotypes, 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

twin–enabled precision oncology is transforming personalized cancer medicine by integrating longitudinal patient data, multi-omics, radiological imaging, digital pathology, laboratory biomarkers, wearable technologies, electronic health records, foundation AI models, and 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 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 digital twin–enabled precision 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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