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MULTIMODAL DIGITAL BIOMARKERS IN ONCOLOGY: ARTIFICIAL INTELLIGENCE FOR EARLY DETECTION AND PERSONALIZED TREATMENT

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Abstract: Digital biomarkers have emerged as one of the most transformative innovations in precision oncology by enabling continuous, objective, and quantitative assessment of cancer biology through integration of multimodal biomedical data. Unlike conventional biomarkers that often rely on isolated molecular or laboratory measurements, multimodal digital biomarkers combine radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, wearable physiological monitoring, laboratory investigations, electronic health records, patient-reported outcomes, and real-world clinical data into comprehensive computational representations of disease. Recent advances in artificial intelligence (AI), particularly foundation models, multimodal transformers, graph neural networks, self-supervised learning, and generative AI, have fundamentally transformed digital biomarker discovery by enabling generalized biomedical representation learning across heterogeneous data modalities. These intelligent systems facilitate early cancer detection, molecular characterization, prognostic prediction, therapeutic response assessment, immunotherapy optimization, adaptive disease monitoring, digital twin simulation, 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 multimodal biomarker ecosystems by enabling collaborative, privacy-preserving, and continuously adaptive computational oncology. Despite remarkable technological progress, important scientific, technical, ethical, and regulatory challenges remain regarding multimodal data harmonization, computational scalability, interoperability, interpretability, cybersecurity, clinical validation, and equitable implementation. This review provides a comprehensive overview of multimodal digital biomarkers in oncology, emphasizing artificial intelligence as the driving force for early cancer detection and personalized treatment.[1]

Keywords: *Digital biomarkers, Artificial intelligence, Precision oncology, Foundation models, Early cancer detection, Personalized medicine, Multimodal learning, Computational oncology, Clinical decision support, Digital health.*

1. Introduction

Cancer is a dynamic biological disease characterized by continuous genomic evolution, epigenetic remodeling, immune adaptation, metabolic reprogramming, tissue remodeling, and complex interactions among malignant cells, stromal components, and host physiology. These biological processes evolve throughout diagnosis, treatment, recurrence, metastasis, and survivorship, necessitating continuous assessment rather than isolated clinical evaluation.[2]

Traditional oncology relies heavily on histopathological examination, laboratory investigations, radiological imaging, and molecular diagnostics performed at discrete clinical time points. Although these methods

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remain indispensable, they often provide only limited snapshots of disease biology and may fail to detect subtle changes associated with early progression, therapeutic resistance, or recurrence.[3]

Recent advances in digital health technologies—including wearable biosensors, high-resolution medical imaging, digital pathology, liquid biopsy, genomic sequencing, electronic health records, and patient-reported outcome systems—have generated unprecedented quantities of longitudinal biomedical information. Artificial intelligence now enables integration of these heterogeneous data into multimodal digital biomarkers capable of continuously characterizing patient-specific disease states.[4]

The convergence of AI, multimodal digital biomarkers, and precision oncology therefore represents a transformative paradigm for early cancer detection, individualized treatment planning, adaptive disease monitoring, and personalized clinical decision-making.[5]

2. Evolution of Digital Biomarkers in Oncology

The concept of biomarkers has evolved considerably over the past several decades. Early oncology biomarkers primarily consisted of serum proteins, histopathological features, and individual molecular alterations associated with diagnosis or prognosis. Although these biomarkers significantly improved cancer management, they frequently lacked sufficient sensitivity, specificity, or dynamic responsiveness for comprehensive precision medicine.[6]

Advances in molecular biology introduced genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, and spatial biology, substantially expanding biological characterization of tumors. Simultaneously, digital pathology, radiomics, wearable physiological monitoring, mobile health technologies, and electronic health records generated increasingly diverse biomedical information.

Artificial intelligence subsequently enabled computational integration of these heterogeneous modalities into unified digital biomarkers, while foundation AI models introduced generalized multimodal representation learning capable of supporting numerous oncology applications beyond individual predictive tasks.

Today, multimodal digital biomarkers represent continuously evolving computational representations reflecting dynamic biological processes throughout the cancer care continuum.[7]

3. Principles of Multimodal Digital Biomarkers

Multimodal digital biomarkers differ fundamentally from conventional biomarkers because they integrate multiple complementary biomedical modalities into unified computational representations rather than relying upon isolated biological measurements. Artificial intelligence serves as the computational framework responsible for harmonizing heterogeneous information across molecular, cellular, tissue, physiological, behavioral, and clinical domains.[8]

Foundation AI models utilize self-supervised learning to discover latent biological relationships without requiring extensive manual annotation, while multimodal transformer architectures align radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, wearable physiological monitoring, physician documentation, and longitudinal clinical records within shared embedding spaces.

Graph neural networks further model interactions among genes, proteins, signaling pathways, imaging phenotypes, physiological variables, therapeutic targets, and clinical outcomes, thereby enabling systems-level computational reasoning supporting precision oncology.[9]

4. Computational Architecture

Modern multimodal digital biomarker platforms consist of interconnected computational layers responsible for multimodal biomedical data acquisition, preprocessing, representation learning, biomarker discovery, predictive analytics, adaptive learning, and intelligent clinical decision support.[10]

The acquisition layer continuously incorporates radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, liquid biopsy, wearable physiological monitoring, medication history,

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patient-reported outcomes, and longitudinal electronic health records. 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 status, behavioral characteristics, and clinical trajectories. These computational representations support downstream biomarker discovery, disease prediction, therapeutic optimization, and adaptive clinical intelligence.[11]

5. Foundation AI Models for Digital Biomarker Discovery

Foundation AI models have fundamentally transformed digital biomarker discovery by learning generalized biomedical representations from massive multimodal datasets before adaptation to specialized oncology applications. Unlike conventional machine learning algorithms developed for isolated predictive tasks, foundation models acquire transferable computational knowledge applicable across diagnosis, prognosis, biomarker discovery, therapeutic prediction, disease monitoring, and intelligent clinical decision support.[12]

Transformer architectures enable multimodal attention across imaging, pathology, molecular biology, laboratory investigations, wearable monitoring, and clinical documentation, while graph neural networks characterize biological 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 the principal engine driving multimodal digital biomarker discovery in precision oncology.[13]

6. Imaging-Based Digital Biomarkers

Radiological imaging provides one of the richest sources of digital biomarkers because medical images contain high-dimensional quantitative information describing tumor morphology, vascularity, metabolism, heterogeneity, spatial organization, and temporal evolution. Foundation AI models automatically extract generalized imaging representations from computed tomography, magnetic resonance imaging, positron emission tomography, ultrasound, and hybrid imaging modalities without requiring handcrafted feature engineering.[14]

Artificial intelligence identifies latent imaging biomarkers associated with molecular alterations, immune infiltration, angiogenesis, fibrosis, hypoxia, therapeutic responsiveness, treatment resistance, and disease progression. Integration of radiological imaging with complementary biomedical modalities substantially improves early diagnosis, prognostic prediction, therapeutic optimization, and longitudinal disease monitoring.

These imaging-derived digital biomarkers provide a non-invasive computational window into evolving tumor biology while strengthening precision oncology.[15]

7. Multi-Omics Digital Biomarkers

Comprehensive digital biomarker discovery increasingly depends upon integration of genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, microbiomics, spatial biology, and single-cell sequencing into unified molecular representations of cancer biology.[16]

Foundation AI models utilize multimodal transformers, graph neural networks, biological knowledge graphs, and self-supervised learning to identify latent relationships among genes, proteins, metabolites, signaling pathways, immune responses, imaging phenotypes, and therapeutic targets that remain difficult to detect using isolated analytical methods.

These integrated molecular biomarkers substantially improve molecular subtype classification, biomarker discovery, therapeutic response prediction, systems biology research, and individualized precision medicine while enabling dynamic characterization of tumor evolution.[17]

8. Wearable Technologies and Physiological Digital Biomarkers

Wearable biosensors and mobile health technologies have expanded digital biomarker discovery beyond traditional hospital-based assessments by continuously monitoring physiological and behavioral parameters throughout the patient journey. Smartwatches, biosensors, implantable devices, and remote monitoring platforms provide longitudinal information regarding physical activity, heart rate, sleep quality, respiratory function, treatment-related symptoms, medication adherence, and quality of life.[18]

Artificial intelligence integrates these real-world physiological data with imaging, molecular diagnostics, laboratory biomarkers, and electronic health records to generate continuously evolving digital biomarkers capable of identifying early clinical deterioration, treatment toxicity, functional decline, recurrence, and disease progression.

These physiological digital biomarkers strengthen patient-centered precision oncology by enabling continuous monitoring outside conventional clinical environments while improving early intervention and personalized supportive care.[19]

9. Artificial Intelligence for Early Cancer Detection

One of the most important clinical applications of multimodal digital biomarkers is early cancer detection through integration of radiological imaging, digital pathology, molecular diagnostics, laboratory investigations, wearable physiological monitoring, electronic health records, and longitudinal clinical trajectories. Foundation AI models identify subtle biological patterns associated with early malignant transformation before clinically apparent disease develops, thereby supporting earlier diagnosis, individualized risk stratification, and timely therapeutic intervention while improving long-term patient outcomes.[20]

10. Digital Biomarkers for Personalized Therapeutics

One of the most clinically significant applications of multimodal digital biomarkers is the personalization of cancer therapy through comprehensive integration of imaging, pathology, molecular biology, physiology, and longitudinal clinical intelligence. Unlike conventional treatment selection based primarily on isolated molecular markers, foundation AI models generate unified patient-specific computational representations capable of capturing the biological complexity underlying therapeutic response.[21]

Artificial intelligence simultaneously analyzes radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, wearable physiological monitoring, medication history, and longitudinal clinical outcomes to predict responsiveness to chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment combinations. These intelligent computational biomarkers further estimate treatment-related toxicity, recurrence probability, progression-free survival, overall survival, and mechanisms of therapeutic resistance while continuously adapting to evolving patient biology.

Such personalized therapeutic intelligence substantially improves precision medicine by enabling individualized treatment selection and dynamic optimization throughout the cancer care continuum.

11. Digital Twins and Biomarker Ecosystems

Digital twin technology represents one of the most advanced applications of multimodal digital biomarkers by integrating heterogeneous biomedical information into continuously evolving virtual representations of individual patients. Foundation AI models combine serial radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, liquid biopsy, wearable physiological monitoring, medication history, and longitudinal clinical information into adaptive computational patient models capable of simulating disease progression and therapeutic response.[22]

Digital biomarkers continuously update these virtual patients, allowing simulation of tumor evolution, immune adaptation, treatment efficacy, toxicity, recurrence, metastatic dissemination, and survival under multiple therapeutic scenarios. By incorporating newly acquired biomedical information in real time, digital twins enable clinicians to compare alternative interventions before implementation while supporting adaptive precision oncology.

These integrated biomarker ecosystems therefore transform digital biomarker analysis from static prediction toward continuously evolving computational medicine.

12. Intelligent Clinical Decision Support

Multimodal digital biomarker platforms provide the computational foundation for intelligent clinical decision-support systems capable of integrating heterogeneous biomedical information into comprehensive patient-centered recommendations. Radiological imaging, digital pathology, molecular diagnostics, laboratory investigations, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and evidence-based clinical guidelines are synthesized into unified computational environments supporting multidisciplinary oncology care.[23]

Interactive clinical dashboards generate individualized biomarker profiles, diagnostic summaries, therapeutic recommendations, toxicity estimates, recurrence probabilities, survival forecasts, and digital twin simulations while facilitating collaboration among oncologists, radiologists, pathologists, surgeons, 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 across the entire patient journey.

13. Continuous Learning and Federated Biomarker Intelligence

The effectiveness of multimodal digital biomarkers depends upon their ability to evolve continuously as new biomedical information becomes available. Artificial intelligence incorporates serial imaging examinations, computational pathology, circulating tumor DNA, laboratory biomarkers, wearable physiological monitoring, medication adherence, patient-reported outcomes, and real-world clinical evidence into adaptive computational frameworks capable of continuously refining biomarker performance and predictive accuracy.[24]

Federated learning further strengthens digital biomarker ecosystems by enabling collaborative development of foundation AI models across geographically distributed healthcare institutions without requiring centralized sharing of sensitive patient information. Participating organizations securely exchange encrypted model parameters while maintaining local control of biomedical datasets, thereby improving algorithm robustness, fairness, external validity, and global applicability.

The combination of continual learning and federated intelligence establishes adaptive biomarker ecosystems capable of supporting worldwide precision oncology while preserving patient privacy and institutional governance.

14. Explainability, Validation, and Ethical Implementation

Successful implementation of multimodal digital biomarkers requires transparent, interpretable, reproducible, and rigorously validated artificial intelligence systems capable of supporting clinician confidence, patient trust, and regulatory approval. Explainable artificial intelligence (XAI) enables clinicians to understand computational 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 predictive outputs.[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 stewardship, and continuous post-deployment surveillance to ensure trustworthy integration of

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digital biomarker technologies into routine oncology practice.

15. Future Perspectives

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

These next-generation computational ecosystems will continuously integrate molecular biology, imaging, 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 biomarker ecosystems are expected to transform oncology from fragmented and reactive disease management toward predictive, preventive, adaptive, continuously learning, and precision-guided healthcare.

16. Discussion

Multimodal digital biomarkers represent one of the most significant paradigm shifts in computational oncology by integrating imaging, pathology, molecular biology, physiology, and longitudinal clinical intelligence into unified computational ecosystems capable of supporting comprehensive personalized cancer care. Unlike conventional biomarkers developed from isolated laboratory or molecular measurements, these intelligent systems simultaneously analyze radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable technologies, and longitudinal clinical trajectories to generate holistic representations of evolving cancer biology.[27]

Applications spanning early cancer detection, biomarker discovery, digital twins, precision immunotherapy, adaptive therapeutics, continuous monitoring, federated collaboration, digital health, survivorship management, and intelligent clinical decision support demonstrate the extraordinary potential of multimodal artificial intelligence to redefine biomarker science. 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 longitudinal healthcare data continue to expand, multimodal digital biomarkers are expected to become a foundational component of future precision oncology.

17. Conclusion

Multimodal digital biomarkers are redefining precision oncology by integrating radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable technologies, electronic health records, digital twins, and longitudinal clinical intelligence into unified computational ecosystems capable of supporting early cancer detection, personalized therapeutics, adaptive disease monitoring, predictive clinical decision-making, and continuously individualized cancer care throughout the disease continuum.[28]

Advances in foundation AI models, transformer architectures, multimodal learning, graph neural networks, self-supervised learning, federated learning, reinforcement learning, digital twins, multimodal large language models, agentic AI, and generative artificial intelligence are expected to further strengthen these intelligent ecosystems, enabling increasingly accurate biomarker discovery, molecular characterization, therapeutic optimization, disease surveillance, and evidence-based precision oncology.[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,

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industry partners, and regulatory agencies will accelerate the responsible implementation of multimodal digital biomarker technologies. 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 oncology worldwide.[30]

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