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DIGITAL BIOMARKERS AND ARTIFICIAL INTELLIGENCE: THE FUTURE OF PRECISION ONCOLOGY AND PERSONALIZED THERAPEUTICS

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Abstract: Digital biomarkers have emerged as a transformative component of precision oncology by enabling continuous, objective, and multidimensional assessment of cancer biology through integration of artificial intelligence (AI), multimodal biomedical data, wearable technologies, imaging, and molecular profiling. Unlike conventional biomarkers that are often measured at isolated time points, digital biomarkers provide dynamic longitudinal information capable of capturing disease evolution, therapeutic response, treatment-related toxicity, and patient physiology throughout the cancer care continuum. Recent advances in foundation AI models, multimodal transformer architectures, graph neural networks, self-supervised learning, reinforcement learning, and generative artificial intelligence have enabled comprehensive integration of radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, electronic health records, patient-reported outcomes, and real-world clinical evidence into unified computational frameworks. These intelligent systems support early cancer detection, biomarker discovery, molecular characterization, prognostic prediction, therapeutic optimization, immunotherapy selection, digital twin simulation, adaptive disease monitoring, and intelligent clinical decision support. Emerging technologies including multimodal large language models, federated learning, retrieval-augmented generation, explainable artificial intelligence, agentic AI, cloud-native healthcare platforms, and Internet of Medical Things (IoMT) technologies further strengthen digital biomarker ecosystems by enabling collaborative, privacy-preserving, transparent, and continuously adaptive biomedical intelligence. Despite remarkable technological advances, 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 biomarkers and artificial intelligence, emphasizing their transformative role in precision oncology and personalized therapeutics.[1]

Keywords: *Digital biomarkers, Artificial intelligence, Precision oncology, Personalized therapeutics, Foundation models, Computational oncology, Digital health, Clinical decision support, Multi-omics, Wearable technologies.*

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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, vascular structures, and host physiology. These interconnected biological processes evolve throughout diagnosis, treatment, recurrence, metastasis, and survivorship, making precision oncology increasingly dependent upon intelligent computational systems capable of 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, biomedical literature, and patient-reported outcomes. Although each modality contributes valuable biological insight, isolated interpretation frequently overlooks dynamic biological relationships governing disease progression, therapeutic response, resistance mechanisms, toxicity, and long-term clinical outcomes.[3]

Artificial intelligence has emerged as a transformative computational technology capable of integrating these heterogeneous biomedical datasets into unified patient-centered representations. Digital biomarkers extend these capabilities by continuously capturing dynamic physiological, molecular, behavioral, and clinical information throughout the patient's disease journey, enabling adaptive precision oncology.

The convergence of digital biomarkers and artificial intelligence therefore establishes a transformative framework for predictive, preventive, personalized, and continuously learning cancer medicine.[4]

2. Evolution of Digital Biomarkers in Oncology

Biomarker research has evolved from conventional laboratory measurements toward intelligent digital ecosystems capable of continuously monitoring disease biology. Early oncology biomarkers primarily consisted of serum proteins, histopathological findings, and genomic alterations measured intermittently during clinical evaluation. Although these biomarkers substantially improved cancer diagnosis and treatment selection, they provided only limited snapshots of continuously evolving biological processes.[5]

Advances in wearable biosensors, digital pathology, radiomics, computational imaging, liquid biopsy, remote patient monitoring, mobile health technologies, and electronic health records substantially expanded the scope of biomarker discovery. Simultaneously, deep learning and transformer architectures enabled automated extraction of high-dimensional digital biomarkers from heterogeneous biomedical data.

Foundation AI models now integrate multimodal digital biomarkers into generalized computational representations supporting diagnosis, prognosis, therapeutic optimization, disease monitoring, and personalized oncology.[6]

3. Principles of Artificial Intelligence–Driven Digital Biomarkers

Artificial intelligence–enabled digital biomarkers differ fundamentally from conventional biomarkers because they continuously integrate multimodal biomedical information into adaptive patient-specific computational representations rather than relying upon isolated measurements. Foundation AI models analyze radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, wearable physiological monitoring, physician documentation, patient-reported outcomes, environmental exposures, and longitudinal clinical trajectories simultaneously.[7]

Self-supervised learning enables discovery of latent biological relationships without requiring extensive manual annotation, while multimodal transformer architectures align heterogeneous biomedical modalities within unified computational embedding spaces. Graph neural networks further characterize interactions among genes, proteins, signaling pathways, immune populations, imaging phenotypes, physiological variables, behavioral characteristics, therapeutic targets, and clinical outcomes.

These computational principles establish continuously evolving digital biomarkers capable of supporting adaptive precision oncology.[8]

4. Computational Architecture

Modern digital biomarker platforms consist of interconnected computational layers responsible for biomedical data acquisition, preprocessing, representation learning, multimodal fusion, adaptive learning, predictive analytics, digital twin simulation, 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, smartphone-derived behavioral information, medication history, physician documentation, patient-reported

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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 continuously collected physiological measurements.

Foundation AI models subsequently generate generalized multimodal embeddings representing molecular biology, tissue architecture, imaging phenotypes, physiological function, behavioral characteristics, and longitudinal clinical trajectories. These unified computational representations support biomarker discovery, diagnosis, prognostic prediction, therapeutic optimization, adaptive learning, and personalized oncology.[10]

5. Imaging-Based Digital Biomarkers

Radiological imaging provides one of the richest sources of digital biomarkers describing tumor morphology, vascularity, metabolism, texture, spatial heterogeneity, and temporal evolution. Foundation AI models automatically extract generalized radiomic representations from computed tomography, magnetic resonance imaging, positron emission tomography, ultrasound, mammography, and hybrid imaging platforms without requiring handcrafted feature engineering.[11]

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 biomarkers with molecular biology and clinical intelligence substantially improves diagnosis, prognostic prediction, biomarker discovery, therapeutic optimization, and longitudinal disease monitoring.

These imaging-derived digital biomarkers provide non-invasive computational windows into evolving tumor biology while strengthening personalized oncology.[12]

6. Molecular Digital Biomarkers

Comprehensive molecular characterization represents one of the greatest strengths of AI-driven digital biomarker ecosystems. Artificial intelligence integrates genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, microbiomics, spatial biology, circulating tumor DNA, and single-cell sequencing into generalized molecular representations capable of continuously characterizing evolving tumor biology across multiple organizational scales.[13]

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

These molecular digital biomarkers enable discovery of molecular subtypes, therapeutic biomarkers, resistance mechanisms, prognostic signatures, minimal residual disease, and novel therapeutic targets while substantially improving individualized precision medicine.[14]

7. Wearable and Physiological Digital Biomarkers

Wearable technologies have introduced a new generation of digital biomarkers capable of continuously monitoring patient physiology outside conventional healthcare settings. Smartwatches, wearable biosensors, mobile health devices, and remote monitoring platforms continuously measure heart rate, physical activity, sleep quality, respiratory rate, oxygen saturation, temperature, medication adherence, symptom burden, and quality-of-life indicators.[15]

Foundation AI models integrate these physiological biomarkers with radiological imaging, molecular biology, laboratory investigations, digital pathology, and longitudinal clinical information using multimodal transformers and graph neural networks. These integrated physiological representations substantially improve prediction of treatment toxicity, functional decline, hospitalization risk, disease progression, survivorship outcomes, and overall quality of life.

Continuous physiological monitoring therefore extends precision oncology beyond hospital-based assessments toward real-time patient-centered care.[16]

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8. Clinical Intelligence Through Electronic Health Records

Electronic health records represent one of the richest longitudinal sources of digital clinical biomarkers available in oncology. Structured laboratory investigations, medication history, pathology reports, treatment timelines, physician documentation, hospitalizations, patient-reported outcomes, survivorship information, and healthcare utilization collectively provide comprehensive patient-level context extending beyond molecular diagnostics.[17]

Foundation AI models employ natural language processing, temporal transformers, and multimodal reasoning architectures to integrate structured and unstructured EHR data with imaging, molecular biology, wearable monitoring, laboratory biomarkers, and physiological information into unified patient-specific computational representations.

These integrated clinical biomarkers substantially improve prognostic prediction, recurrence surveillance, toxicity estimation, therapeutic optimization, survivorship management, and evidence-based clinical decision-making.[18]

9. Digital Biomarkers for Personalized Therapeutics

One of the most clinically significant applications of artificial intelligence–enabled digital biomarkers is individualized therapeutic optimization through continuous integration of molecular biology, imaging phenotypes, histopathological characteristics, laboratory biomarkers, wearable physiological monitoring, behavioral characteristics, medication history, physician documentation, 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, physiological adaptation, and real-world clinical outcomes. These adaptive computational systems establish continuously evolving digital biomarkers capable of supporting personalized therapeutics throughout the entire cancer care continuum.[19][20]

10. Digital Twins and Dynamic Biomarker Modeling

Digital twin technology represents one of the most transformative applications of artificial intelligence–enabled digital biomarkers by creating continuously evolving virtual representations of individual cancer patients synchronized with their biological counterparts. Foundation AI models integrate serial radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, medication history, patient-reported outcomes, and longitudinal clinical information into adaptive computational patient models capable of simulating disease progression, therapeutic response, treatment-related toxicity, recurrence, metastatic dissemination, and survival.[21]

Unlike conventional predictive models, digital twins continuously update their computational representations as new digital biomarker information becomes available. Integration of physiological monitoring, molecular biomarkers, imaging-derived biomarkers, and behavioral information enables virtual patients to simulate evolving disease trajectories, therapeutic responsiveness, and mechanisms of treatment resistance. These intelligent virtual patients allow clinicians to evaluate multiple therapeutic strategies before implementation, optimize treatment sequencing, anticipate adverse events, and personalize supportive care according to continuously evolving patient biology.

By combining multimodal digital biomarkers with predictive simulation, digital twins transform computational oncology from retrospective analysis toward proactive and continuously adaptive precision medicine.

11. Intelligent Clinical Decision Support

Artificial intelligence–enabled digital biomarkers 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

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physiological monitoring, medication history, physician documentation, patient-reported outcomes, and evidence-based clinical guidelines independently, foundation AI models synthesize these diverse biomedical information sources into unified computational representations supporting multidisciplinary oncology practice.[22]

Interactive clinical dashboards generate individualized diagnostic summaries, digital biomarker analyses, molecular interpretations, digital twin simulations, therapeutic recommendations, toxicity estimates, recurrence probabilities, disease progression forecasts, survival predictions, and longitudinal treatment response assessments 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.

12. Continuous Learning and Adaptive Biomarker Intelligence

A defining characteristic of artificial intelligence–enabled digital biomarker ecosystems is the 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, behavioral information, patient-reported outcomes, biomedical literature, and real-world clinical evidence into adaptive computational frameworks capable of continuously refining predictive accuracy throughout the patient's clinical journey.[23]

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 biomarker platforms remain synchronized with evolving tumor biology, physiological adaptation, emerging scientific discoveries, changing clinical guidelines, and diverse patient trajectories.

This adaptive computational paradigm transforms oncology into a continuously learning healthcare ecosystem capable of supporting real-time personalized precision medicine.

13. Federated Digital Biomarker Networks

Development of highly generalizable digital biomarker models requires access to diverse biomedical datasets representing multiple healthcare systems, imaging platforms, pathology laboratories, molecular technologies, wearable device ecosystems, treatment protocols, and patient populations. Federated learning enables collaborative development of foundation AI models while preserving patient privacy and institutional governance through decentralized computational training.[24]

Participating healthcare institutions independently train local biomarker models using radiological imaging, digital pathology, genomics, transcriptomics, 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, transparency, and generalizability across diverse healthcare environments.

Federated digital biomarker ecosystems therefore establish international computational oncology networks capable of accelerating scientific discovery, improving equitable access to precision medicine, and supporting global cancer research while maintaining responsible biomedical data stewardship.

14. Explainability, Validation, and Ethical Governance

Successful implementation of artificial intelligence–enabled digital biomarkers 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 computational reasoning through attention visualization, saliency maps, SHAP (Shapley Additive Explanations), feature attribution analysis, uncertainty estimation, temporal biomarker visualization, and counterfactual explanations identifying the imaging, molecular, physiological, behavioral, and clinical variables responsible for 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 governance, continuous post-deployment surveillance, and multidisciplinary oversight to ensure trustworthy integration of digital biomarker technologies into routine oncology practice.

15. Future Perspectives

Future digital biomarker ecosystems will increasingly integrate multimodal foundation models, multimodal large language models, agentic artificial intelligence, graph neural networks, reinforcement learning, federated learning, digital twins, spatial multi-omics, single-cell sequencing, liquid biopsy, quantum computing, Internet of Medical Things (IoMT), robotics, and cloud-native healthcare infrastructure into unified 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, continuously synthesizing biomedical evidence, and identifying emerging digital biomarkers associated with disease evolution.

Such intelligent ecosystems are expected to transform oncology from fragmented and reactive disease management toward predictive, preventive, adaptive, continuously learning, and precision-guided healthcare across the global cancer community.

16. Discussion

Artificial intelligence–enabled digital biomarkers represent one of the most significant paradigm shifts in computational oncology by integrating molecular biology, radiological imaging, digital pathology, laboratory biomarkers, wearable technologies, behavioral monitoring, digital twins, and longitudinal clinical intelligence into unified computational ecosystems capable of supporting comprehensive personalized cancer care. Unlike conventional biomarkers measured at isolated time points, digital biomarkers continuously capture evolving biological, physiological, behavioral, and clinical information, enabling dynamic characterization of disease progression, therapeutic response, toxicity, and survivorship.[27]

Applications spanning computational pathology, radiogenomics, biomarker discovery, digital twins, precision immunotherapy, adaptive therapeutics, remote patient monitoring, continuous learning, federated collaboration, digital health, survivorship management, and intelligent clinical decision support demonstrate the extraordinary potential of digital biomarkers 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, digital biomarkers are expected to become one of the foundational computational infrastructures supporting precision oncology worldwide.

17. Conclusion

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

Advances in 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 intelligent biomarker ecosystems, enabling increasingly accurate molecular characterization, predictive clinical decision-making, adaptive therapeutics, continuous disease surveillance, and continuously personalized 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 artificial intelligence–enabled digital biomarkers. 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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