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Artificial Intelligence, Digital Biomarkers, and Precision Oncology: Emerging Technologies for Early Detection and Personalized Intervention

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ABSTRACT

Cancer remains a leading cause of global morbidity and mortality, highlighting the urgent need for earlier diagnosis, accurate risk stratification, and individualized therapeutic strategies. Advances in artificial intelligence (AI) and digital biomarkers have transformed oncology by enabling the integration of molecular, imaging, and clinical data into comprehensive computational frameworks for precision cancer care. Digital biomarkers—including circulating tumor DNA (ctDNA), circulating tumor cells, radiomic signatures, computational pathology, wearable sensor data, and multi-omics profiles—provide dynamic and minimally invasive measures of tumor biology throughout the disease continuum. Simultaneously, deep learning, transformer architectures, foundation models, and multimodal AI have substantially improved the extraction of clinically meaningful information from heterogeneous biomedical datasets. Recent studies demonstrate that AI-assisted liquid biopsy, radiomics, and computational pathology significantly enhance early cancer detection, prognostic assessment, treatment selection, and longitudinal monitoring compared with conventional diagnostic approaches. Emerging technologies such as federated learning, explainable AI, digital twins, and autonomous clinical decision-support systems further facilitate secure, interpretable, and personalized oncology. Nevertheless, widespread clinical implementation remains limited by challenges related to data heterogeneity, algorithmic bias, model interpretability, regulatory approval, interoperability, and prospective clinical validation. This review provides a comprehensive overview of AI-enabled digital biomarkers across the oncology continuum, discusses recent advances in multimodal data integration and computational intelligence, and examines future directions toward adaptive, patient-centered precision oncology. Continued collaboration among clinicians, computational scientists, regulatory agencies, and healthcare systems will be essential to translate these technologies into routine clinical practice while ensuring safety, equity, and clinical effectiveness.

Keywords: *Artificial intelligence; digital biomarkers; precision oncology; liquid biopsy; radiomics; computational pathology; multi-omics; deep learning; foundation models; explainable AI; federated learning; digital twins.*

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1. Introduction

Cancer continues to represent one of the greatest global public health challenges, with millions of new diagnoses and cancer-related deaths occurring each year despite substantial advances in prevention, diagnosis, and treatment [1]. Clinical outcomes remain strongly dependent on early detection and accurate characterization of tumor biology, yet conventional diagnostic approaches—including tissue biopsy,

histopathology, and anatomical imaging—often provide only limited insight into the molecular heterogeneity and dynamic evolution of malignant disease [2]. The growing recognition that tumors evolve continuously during progression and treatment has accelerated the transition from conventional oncology toward precision oncology, where therapeutic decisions are increasingly guided by integrated molecular, pathological, imaging, and clinical information rather than anatomical staging alone [3].

Central to this transformation is the emergence of digital biomarkers, computationally derived quantitative indicators obtained from medical imaging, liquid biopsy, multi-omics profiling, wearable technologies, and electronic health records [4]. Unlike traditional biomarkers that frequently rely on single biological measurements, digital biomarkers integrate multiple sources of biological information to provide continuous, individualized assessment of tumor behavior. Liquid biopsy technologies analyzing circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), extracellular vesicles, and cell-free RNA enable minimally invasive monitoring of tumor evolution, whereas radiomics and computational pathology quantify imaging and histological characteristics that reflect underlying molecular alterations [5]. Together, these technologies enable longitudinal characterization of cancer biology throughout diagnosis, treatment, and survivorship.

Artificial intelligence has emerged as the computational engine that converts these multidimensional datasets into clinically actionable knowledge [6]. Modern machine learning and deep learning algorithms can identify highly complex relationships among molecular, imaging, pathological, and clinical variables that remain inaccessible to conventional statistical methods. Recent advances in transformer architectures, self-supervised learning, multimodal foundation models, and large language models have further expanded AI's ability to integrate heterogeneous biomedical data while improving generalizability across multiple cancer types and healthcare settings [7]. Consequently, AI is increasingly supporting early cancer detection, molecular classification, prognostic prediction, treatment optimization, and continuous disease monitoring through data-driven clinical decision support.

Despite remarkable technological progress, important barriers continue to impede widespread clinical implementation. Performance variability across institutions, limited external validation, algorithmic bias, lack of model transparency, regulatory uncertainty, and challenges associated with interoperability and data governance remain significant obstacles to routine adoption [8]. Addressing these limitations requires not only continued methodological innovation but also standardized validation frameworks, explainable AI methodologies, privacy-preserving collaborative learning strategies, and multidisciplinary clinical evaluation.

This review critically examines the rapidly evolving landscape of AI-enabled digital biomarkers in oncology. We summarize current advances in computational pathology, radiomics, liquid biopsy, multi-omics integration, and multimodal artificial intelligence while discussing emerging technologies—including foundation models, federated learning, digital twins, and explainable AI—that are shaping the future of precision and preventive oncology. Finally, we highlight the translational, ethical, and regulatory challenges that must be overcome to realize the full clinical potential of AI-driven cancer care.

1. Evolution of Artificial Intelligence in Oncology

Artificial intelligence has evolved from conventional statistical learning algorithms to sophisticated deep learning systems capable of extracting clinically meaningful information directly from high-dimensional biomedical data [9]. Early oncology applications primarily relied on traditional machine learning methods—including logistic regression, support vector machines, random forests, and decision trees—which required manually engineered features derived from medical images, genomic profiles, or clinical datasets. Although these models provided interpretable predictions, their performance was constrained by dependence on expert-defined features and limited ability to capture the complex nonlinear interactions characteristic of cancer biology [10].

The introduction of deep learning fundamentally transformed computational oncology by enabling automatic hierarchical feature learning from raw biomedical data. Convolutional neural networks (CNNs) rapidly became the dominant architecture for medical image analysis, demonstrating expert-level performance in radiological interpretation, computational pathology, tumor segmentation, and metastatic lesion detection [11]. Rather than relying on handcrafted descriptors, CNNs progressively learn increasingly abstract image representations that capture diagnostically and prognostically relevant characteristics beyond human visual perception.

Subsequent developments expanded AI capabilities beyond static image analysis. Recurrent neural networks enabled temporal modeling of longitudinal clinical and biomarker data, whereas attention mechanisms improved model performance by selectively focusing on clinically relevant regions of images or sequential data [12]. More recently, transformer architectures have emerged as the leading paradigm for biomedical AI because of their ability to model long-range dependencies and efficiently integrate heterogeneous multimodal information. Vision Transformers have demonstrated superior robustness across diverse imaging protocols and improved transfer learning capabilities, particularly when adapted from large-scale pretrained models [13].

An equally important advancement has been the emergence of foundation models and large language models (LLMs) trained on massive multimodal biomedical datasets [14]. These pretrained models provide generalized representations that can be efficiently adapted to specialized oncology tasks using relatively small annotated datasets, substantially reducing development time and improving performance in rare cancers and resource-limited settings. Simultaneously, transformer-based language models have enabled automated extraction of clinically relevant information from pathology reports, radiology narratives, genomic reports, and electronic health records, facilitating comprehensive integration of structured and unstructured clinical information [15].

Collectively, these developments reflect a transition from isolated task-specific AI systems toward unified

multimodal computational platforms capable of supporting diagnosis, prognosis, treatment selection, and continuous learning across the entire oncology care pathway.

2. Digital Biomarkers in Oncology: Definition, Classification, and Clinical Applications

Digital biomarkers are computationally derived quantitative indicators obtained from biological samples, medical imaging, physiological monitoring, and digital health technologies that provide objective measurements of disease status, therapeutic response, and clinical outcomes [16]. Within oncology, these biomarkers represent a rapidly expanding class of measurable indicators that integrate molecular, imaging, physiological, and clinical information through advanced computational analysis to support precision cancer management.

Digital biomarkers encompass several complementary categories. Liquid biopsy biomarkers, including circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), extracellular vesicles, cell-free RNA, and circulating proteins, enable minimally invasive molecular characterization and longitudinal monitoring of tumor evolution [18]. Radiomic biomarkers quantify tumor morphology, texture, vascularity, and spatial heterogeneity from CT, MRI, PET, and ultrasound images, whereas computational pathology extracts quantitative morphological and spatial features from whole-slide histopathology images using deep learning algorithms [19]. Molecular biomarkers derived from genomics, transcriptomics, proteomics, metabolomics, and epigenomics provide detailed characterization of oncogenic pathways, therapeutic targets, and mechanisms of treatment resistance [20]. Additionally, wearable devices and digital health technologies continuously monitor physiological parameters—including physical activity, sleep quality, heart rate variability, and functional status—that may reflect treatment toxicity, disease progression, or declining patient health [17].

The greatest clinical value of digital biomarkers arises from their integration within multimodal AI frameworks. Longitudinal biomarker trajectories frequently provide substantially greater prognostic information than isolated measurements, allowing AI systems to identify subtle biological changes preceding radiological progression or clinical deterioration [22]. Integration of liquid biopsy, imaging biomarkers, computational pathology, molecular profiling, and wearable-derived physiological data consistently demonstrates superior predictive performance compared with single-modality approaches, reflecting the multidimensional nature of tumor biology and reinforcing the central role of multimodal AI in precision oncology [23].

3. Artificial Intelligence Architectures in Oncology

Artificial intelligence in oncology encompasses a broad spectrum of computational architectures designed to address diverse clinical tasks and heterogeneous biomedical data. Traditional machine learning (ML) algorithms—including support vector machines (SVMs), random forests, logistic regression, and gradient-boosting methods such as XGBoost, LightGBM, and CatBoost—remain highly effective for structured datasets derived from electronic health records, laboratory investigations, genomic features, and clinical variables [24]. Their relatively high interpretability, feature importance analysis, and transparent decision-making processes make these algorithms particularly valuable in clinical settings where explainability is essential for physician acceptance and regulatory approval.

The emergence of deep learning (DL) has significantly expanded the capabilities of AI in oncology by enabling automatic feature extraction from high-dimensional biomedical data. Convolutional neural networks (CNNs) have become the foundation of medical image analysis owing to their ability to identify hierarchical spatial patterns within radiological and histopathological images [25]. Recurrent neural networks (RNNs) and long short-term memory (LSTM) architectures have been successfully applied to longitudinal clinical datasets, facilitating temporal modeling of disease progression, treatment response, and biomarker dynamics. In parallel, graph neural networks (GNNs) have enabled sophisticated analysis of biological interaction networks, tumor microenvironment architecture, and cell–cell communication by representing complex biological systems as interconnected graph structures.

More recently, transformer architectures have revolutionized oncology AI through the use of self-attention mechanisms capable of modeling long-range relationships within imaging, molecular, and clinical data [26]. Vision Transformers (ViTs) have demonstrated state-of-the-art performance in radiology and computational pathology by capturing global contextual information that often exceeds the capabilities of conventional convolution-based models. Their ability to learn complex spatial relationships has significantly improved tumor detection, tissue classification, and prognostic prediction across multiple cancer types.

A major advancement in recent years has been the development of foundation models, which are pretrained on extremely large and diverse biomedical datasets before being adapted to specific clinical applications through transfer learning [27]. Examples include transformer-based language models derived from BERT for clinical text processing and large Vision Transformer models for computational pathology and radiology. These pretrained models require comparatively small task-specific datasets to achieve excellent performance, thereby addressing one of the major limitations of medical AI—the scarcity of high-quality annotated data.

Complementing foundation models, self-supervised learning and contrastive learning enable AI systems to learn robust feature representations directly from unlabeled biomedical datasets, substantially reducing dependence on labor-intensive expert annotation [28]. This capability is particularly valuable in oncology, where annotation of pathology slides, genomic datasets, and radiological images requires extensive specialist expertise.

The evolution toward multimodal AI further reflects the recognition that cancer is inherently a complex systems disease requiring simultaneous analysis of multiple biological domains. Contemporary multimodal frameworks employ dedicated encoders for imaging, genomics, pathology, laboratory biomarkers, and clinical records before integrating these representations through

attention-based fusion networks [29]. Such architectures consistently outperform single-modality models because they capture complementary biological information spanning molecular, cellular, tissue, and clinical levels.

Collectively, the evolution from traditional machine learning toward foundation models and multimodal transformer-based systems marks a significant shift toward unified computational platforms capable of delivering comprehensive, interpretable, and clinically scalable precision oncology.

4. AI in Early Cancer Detection

Early cancer detection remains one of the most impactful applications of artificial intelligence because diagnosis during localized disease stages substantially improves treatment success, long-term survival, and overall patient outcomes [30]. AI-powered diagnostic systems integrate radiological imaging, computational pathology, liquid biopsy, and molecular biomarkers to detect malignancies at earlier stages than conventional diagnostic approaches while reducing false-positive findings and unnecessary invasive procedures.

Within radiology, deep learning algorithms have demonstrated diagnostic performance comparable to—or exceeding—that of experienced radiologists for multiple cancer screening applications, including mammography, low-dose computed tomography (LDCT), magnetic resonance imaging (MRI), and colorectal imaging [31]. AI systems trained on large mammographic datasets improve breast cancer detection sensitivity by approximately 10–15% while simultaneously decreasing false-positive recall rates. These improvements arise from the ability of deep learning models to identify subtle imaging characteristics—including architectural distortion, microcalcification patterns, tissue asymmetry, and textural heterogeneity—that frequently remain below the threshold of human visual perception.

Artificial intelligence has similarly transformed computational pathology through automated analysis of whole-slide histopathological images. Deep learning models accurately identify metastatic deposits within lymph nodes with sensitivities exceeding 99%, quantify mitotic activity, evaluate nuclear atypia, assess tumor differentiation, and predict molecular subtypes directly from routine hematoxylin and eosin (H&E)-stained tissue sections [32]. These capabilities reduce interobserver variability, standardize pathological interpretation, and provide quantitative biomarkers that support diagnosis, prognostic assessment, and therapeutic planning.

Another rapidly advancing area involves liquid biopsy, where machine learning algorithms analyze complex circulating biomarker profiles to facilitate minimally invasive early cancer detection. Multi-cancer early detection (MCED) assays integrating circulating tumor DNA (ctDNA), circulating proteins, methylation patterns, and other plasma biomarkers have demonstrated encouraging sensitivity for identifying multiple malignancies in asymptomatic individuals, with detection performance increasing according to disease stage [33]. Detecting ctDNA during early-stage disease remains technically challenging because circulating tumor-derived DNA frequently constitutes less than 0.1% of total circulating cell-free DNA. Advances in fragmentomics, methylation profiling, and sophisticated error-correction algorithms have substantially improved analytical sensitivity by distinguishing tumor-derived DNA fragments from background hematopoietic cell-free DNA with remarkable precision [34].

Increasingly, multi-omics integration has emerged as a powerful strategy for improving early detection. Artificial intelligence combines genomic mutations, DNA methylation patterns, transcriptomic signatures, proteomic biomarkers, metabolomic profiles, and imaging features into unified predictive models capable of identifying cancer before clinical symptoms develop [35]. For example, integrated analysis of whole-genome sequencing, methylation profiling, and circulating plasma proteins has demonstrated high sensitivity for detecting early-stage pancreatic cancer among high-risk populations, substantially outperforming individual biomarker modalities. Similarly, radiogenomic approaches combining radiomic imaging features with genomic information enable prediction of tumor genotype, molecular subtype, and treatment responsiveness without requiring invasive tissue biopsy [36].

Collectively, AI-enabled multimodal early detection strategies are transforming oncology from reactive diagnosis toward proactive cancer interception by enabling earlier diagnosis, more accurate risk assessment, and personalized screening approaches.

5. Personalized Oncology and Therapeutic Decision-Making

Precision oncology aims to deliver individualized cancer treatment by tailoring therapeutic strategies according to each patient's unique molecular, pathological, and clinical characteristics [37]. Artificial intelligence plays a central role in achieving this objective by integrating genomic, transcriptomic, imaging, pathological, and clinical data to predict therapeutic response, optimize treatment selection, and improve long-term patient outcomes.

Machine learning models trained on tumor genomic profiles, transcriptomic signatures, and large-scale pharmacogenomic datasets can accurately predict sensitivity to chemotherapy, targeted therapy, and combination treatment regimens, thereby reducing reliance on empirical therapeutic selection [38]. These predictive models identify actionable molecular targets while estimating the probability of response to individual therapeutic agents, enabling clinicians to personalize treatment according to each patient's tumor biology.

AI has demonstrated particularly significant value within immuno-oncology. Computational models integrating tumor mutational burden (TMB), microsatellite instability (MSI), programmed death-ligand 1 (PD-L1) expression, neoantigen burden, immune cell infiltration, and genomic alterations accurately predict responsiveness to immune checkpoint inhibitors [39]. By distinguishing likely responders from non-responders before treatment initiation, these models improve patient selection, maximize therapeutic benefit, and minimize unnecessary treatment-related toxicity.

Artificial intelligence has also substantially improved prognostic prediction by integrating multimodal information that extends beyond conventional TNM staging systems [40]. Deep learning models simultaneously analyze radiological imaging,

computational pathology, genomic alterations, clinical variables, and longitudinal biomarker trajectories to generate individualized predictions of recurrence, metastasis, and overall survival. In breast cancer, for example, multimodal AI models combining histopathological imaging, molecular profiling, and radiological features have demonstrated greater prognostic accuracy than traditional staging systems and established genomic assays, thereby supporting more precise decisions regarding adjuvant chemotherapy and long-term surveillance.

An emerging application involves adaptive treatment planning, where longitudinal monitoring of digital biomarkers enables continuous optimization of therapeutic strategies throughout the treatment course [41]. Serial assessment of circulating tumor DNA, imaging biomarkers, and molecular signatures allows AI systems to identify emerging drug resistance before radiological progression becomes clinically apparent. Early recognition of molecular relapse enables timely modification of therapeutic regimens, potentially delaying or preventing treatment failure associated with acquired resistance.

Artificial intelligence has further enhanced patient stratification by applying unsupervised machine learning techniques to identify previously unrecognized molecular subtypes characterized by distinct biological behavior, prognostic profiles, and therapeutic vulnerabilities [42]. These computationally derived tumor subgroups frequently provide superior prognostic discrimination compared with conventional clinicopathological classification, highlighting biologically meaningful heterogeneity that remains undetected by traditional diagnostic approaches.

Increasingly, precision oncology trials utilize AI-assisted molecular profiling to match patients with targeted therapies based on comprehensive genomic characterization. Early evidence suggests that genomically matched treatment strategies substantially improve response rates compared with conventional treatment selection, particularly when molecular matching is combined with AI-based prediction of functional drug sensitivity rather than reliance on genomic alterations alone [43].

Overall, AI-driven personalized oncology is transforming cancer care by enabling data-driven therapeutic decision-making, adaptive treatment optimization, individualized prognostic assessment, and more precise allocation of targeted therapies, thereby advancing the realization of truly personalized cancer medicine.

6. Explainable AI and Clinical Interpretability

The successful integration of artificial intelligence into routine oncology practice depends not only on predictive performance but also on transparency, interpretability, and clinician trust. Many advanced machine learning models—particularly deep neural networks—operate as complex “black-box” systems, producing highly accurate predictions while providing limited insight into the reasoning underlying their decisions [44]. This lack of interpretability poses a significant challenge in oncology, where diagnostic and therapeutic recommendations directly influence patient survival, treatment-related toxicity, and long-term clinical outcomes.

Explainable artificial intelligence (XAI) has emerged as a critical strategy for improving the transparency of AI-assisted clinical decision-making. XAI encompasses a range of techniques that enable clinicians to understand the contribution of individual variables to model predictions. Model-agnostic methods such as Shapley Additive exPlanations (SHAP) and Local Interpretable Model-Agnostic Explanations (LIME) quantify feature importance and identify the clinical variables that most strongly influence individual predictions [45]. In medical imaging, visualization approaches including Gradient-weighted Class Activation Mapping (Grad-CAM), attention heatmaps, and saliency mapping identify anatomical regions or histopathological structures that contribute most significantly to diagnostic classification, thereby allowing clinicians to verify that AI systems focus on biologically meaningful features.

Application of these explainability methods has generated both encouraging and cautionary findings. Numerous studies demonstrate that AI models frequently identify clinically relevant imaging features such as tumor margins, intratumoral heterogeneity, and characteristic histopathological patterns that align with expert clinical interpretation [46]. However, explainability analyses have also revealed instances in which AI systems inadvertently rely on imaging artifacts, scanner-specific characteristics, or other confounding variables unrelated to disease biology, emphasizing the importance of systematic model validation before clinical deployment.

Clinical studies indicate that incorporating explainable AI significantly improves physician confidence and acceptance of AI-generated recommendations. Radiologists and pathologists provided with visual explanations accompanying AI predictions demonstrate greater trust in algorithmic decision-making and are more likely to incorporate AI outputs into routine clinical practice than when predictions are presented without supporting explanations [47]. These observations underscore that interpretability is not merely a desirable feature but an essential prerequisite for safe clinical implementation.

Explainable AI has also become an important tool for identifying algorithmic bias. Analyses of diagnostic AI systems have demonstrated that model performance may vary across patient populations defined by age, sex, ethnicity, socioeconomic status, or healthcare setting, indicating that algorithms may unintentionally learn demographic associations unrelated to disease biology [48]. These findings have stimulated the development of fairness-aware machine learning approaches that explicitly minimize reliance on sensitive demographic attributes while preserving predictive accuracy. Consequently, the integration of explainability, fairness assessment, and bias mitigation has become a central component of responsible AI development in precision oncology.

7. Federated Learning and Privacy-Preserving Oncology AI

The development of high-performing AI systems for oncology requires access to large, diverse, and representative clinical datasets encompassing medical imaging, genomic sequencing, pathology, laboratory investigations, and longitudinal patient outcomes.

However, privacy regulations—including the General Data Protection Regulation (GDPR) and the Health Insurance Portability and Accountability Act (HIPAA)—significantly restrict centralized sharing of sensitive patient information [49]. This creates a fundamental challenge in oncology AI: the need for collaborative model development while preserving patient privacy and institutional autonomy.

Federated learning (FL) has emerged as an effective solution to this challenge by enabling decentralized model training across multiple healthcare institutions without transferring raw patient data [50]. Within the federated learning framework, each participating institution trains a local AI model using its own clinical data. Only model parameters or encrypted gradient updates are transmitted to a central server, where they are aggregated to produce an improved global model before being redistributed to participating institutions. Throughout this process, patient-level information remains securely within local institutional servers, thereby maintaining compliance with privacy regulations.

Federated learning has demonstrated encouraging results across multiple oncology applications. Multicenter studies involving brain tumor classification, computational pathology, radiomics, and cancer outcome prediction have shown that federated models achieve diagnostic accuracy comparable to centrally trained models while preserving complete data locality [51]. Additional privacy-preserving techniques, including differential privacy, secure aggregation, and homomorphic encryption, further strengthen data protection by preventing reconstruction of individual patient information from transmitted model updates, although these approaches may introduce modest reductions in predictive performance [52].

Beyond privacy preservation, federated learning offers several important advantages for clinical translation. AI models developed within single institutions frequently demonstrate reduced performance when applied to external healthcare systems because of differences in imaging protocols, patient demographics, disease prevalence, laboratory methodologies, and clinical workflows [53]. Training across geographically and clinically diverse institutions naturally improves model robustness, external validity, and generalizability while reducing the effects of domain shift. Moreover, federated learning simplifies multicenter collaboration by reducing administrative barriers associated with conventional data-sharing agreements and institutional governance requirements [54].

Future developments are expected to combine federated learning with explainable AI to produce decentralized models that not only protect patient privacy but also generate transparent, clinically interpretable predictions suitable for physician review [55]. Nevertheless, important technical challenges remain, including communication overhead associated with frequent model synchronization, heterogeneity of institutional computing resources, differences in local data quality, and the need for standardized interoperability frameworks compatible with diverse electronic health record systems. Addressing these challenges will be essential for widespread adoption of privacy-preserving AI across international oncology networks.

8. Future Perspectives: Digital Twins, Autonomous Systems, and Real-World Evidence Integration

Rapid advances in artificial intelligence are expanding the future of precision oncology beyond predictive analytics toward adaptive, continuously learning healthcare systems. Among the most promising developments are digital twins, autonomous clinical decision-support systems, multimodal foundation models, and real-world evidence (RWE)-driven learning frameworks, each of which has the potential to fundamentally transform personalized cancer care [56].

Digital twins represent virtual computational replicas of individual patients that continuously integrate radiological imaging, multi-omics data, histopathology, treatment history, physiological monitoring, and longitudinal biomarker trajectories to simulate disease progression and therapeutic response [57]. By modeling tumor biology at molecular, cellular, and tissue levels, digital twins provide an opportunity to evaluate multiple therapeutic strategies in silico before clinical implementation. Rather than relying on sequential empirical treatment adjustments after disease progression occurs, digital twin technology could enable prospective optimization of treatment sequencing, prediction of emerging drug resistance, and individualized therapy selection based on patient-specific biological simulations.

Another emerging concept involves autonomous oncology systems, in which AI continuously analyzes multimodal patient data—including wearable biosensors, liquid biopsy results, medical imaging, laboratory investigations, and electronic health records—to monitor disease evolution and generate real-time treatment recommendations [58]. Although fully autonomous clinical decision-making remains a long-term objective, current research increasingly focuses on human-in-the-loop frameworks in which AI provides continuous decision support while clinicians retain ultimate responsibility for diagnosis and therapeutic decisions. Such systems emphasize transparency, explainability, ethical oversight, and regulatory compliance to ensure safe implementation within routine clinical practice [59].

The continued evolution of multimodal foundation models is expected to further accelerate AI-enabled precision oncology. Large-scale pretrained models capable of simultaneously processing radiological images, computational pathology, genomic sequencing, electronic health records, and biomedical literature will provide unified representations that support a broad spectrum of clinical tasks without requiring separate task-specific AI systems [60]. These highly generalizable models are anticipated to improve scalability, reduce development costs, and facilitate deployment across diverse healthcare environments.

Simultaneously, increasing integration of real-world evidence (RWE) into AI systems is reshaping clinical research and therapeutic evaluation. Beyond conventional randomized controlled trials, AI now enables analysis of retrospective observational datasets, wearable-derived physiological information, patient-reported outcomes, electronic health records, and digital health platforms to evaluate treatment effectiveness under routine clinical conditions [61]. Real-world evidence complements traditional clinical trials by

capturing broader patient populations, greater biological diversity, and long-term treatment outcomes that are often underrepresented in highly controlled research settings. Integration of RWE with advanced machine learning therefore provides a more comprehensive understanding of treatment effectiveness, safety, healthcare utilization, and patient quality of life.

Collectively, digital twins, autonomous AI systems, multimodal foundation models, and real-world evidence integration represent the next generation of intelligent oncology ecosystems. Their successful implementation will require continued advances in computational methodology, rigorous prospective validation, standardized regulatory frameworks, robust ethical governance, and close collaboration among clinicians, computational scientists, healthcare organizations, and policymakers to ensure that these transformative technologies improve patient care while maintaining safety, transparency, and equity.

10. Discussion

This review highlights the transformative role of artificial intelligence (AI) and digital biomarkers in reshaping contemporary oncology from a predominantly reactive discipline toward a predictive, personalized, and preventive model of cancer care. The integration of AI with liquid biopsy technologies, radiomics, computational pathology, multi-omics profiling, and wearable health data has substantially enhanced the accuracy of early cancer detection, prognostic prediction, therapeutic selection, and longitudinal disease monitoring. Advanced computational approaches—including deep learning, transformer architectures, foundation models, and multimodal AI—have demonstrated an unprecedented ability to extract clinically meaningful information from complex molecular, imaging, and clinical datasets that often exceeds the analytical capacity of conventional statistical methods and human interpretation.

A recurring theme throughout the literature is that **multimodal integration consistently outperforms single-modality analysis**. Combining genomic, transcriptomic, radiomic, pathological, clinical, and digital health biomarkers enables AI systems to capture complementary biological information across multiple levels of tumor organization, thereby improving diagnostic precision, individualized risk stratification, prediction of treatment response, and clinical outcome assessment. This systems-level approach reflects the inherently heterogeneous nature of cancer and represents a significant advancement toward truly personalized oncology.

Despite these remarkable technological achievements, important translational challenges continue to limit routine clinical implementation. Many AI models remain dependent on retrospective, single-center datasets that lack demographic diversity and external validation. Variability in imaging protocols, biomarker assays, sequencing technologies, and institutional workflows further limits model reproducibility and generalizability across healthcare settings. Moreover, the limited interpretability of complex deep learning models continues to hinder clinician confidence and regulatory acceptance, particularly in high-stakes clinical decision-making. Consequently, explainable AI has emerged as a critical component of trustworthy clinical AI by improving transparency, facilitating clinical validation, and supporting responsible implementation.

The review also underscores the growing importance of **privacy-preserving AI frameworks**, including federated learning, differential privacy, and secure collaborative model development. These technologies enable multicenter AI training without centralizing sensitive patient data, thereby improving model robustness while maintaining compliance with evolving privacy regulations. In parallel, emerging innovations—including digital twins, multimodal foundation models, autonomous clinical decision-support systems, and continuous digital biomarker monitoring—are expected to further transform precision oncology by enabling adaptive, real-time, patient-specific therapeutic optimization.

Ultimately, successful clinical translation will depend on rigorous prospective validation, standardized methodological frameworks, transparent regulatory pathways, ethical governance, and sustained collaboration among clinicians, computational scientists, healthcare institutions, industry partners, and policymakers. Addressing these challenges will be essential to ensure that AI-driven oncology technologies are safe, equitable, clinically effective, and accessible across diverse healthcare environments.

11. Conclusion

The convergence of artificial intelligence and digital biomarkers is fundamentally transforming oncology by enabling comprehensive, minimally invasive, and data-driven approaches to cancer diagnosis, prognostic assessment, treatment selection, and longitudinal disease monitoring. Integration of liquid biopsy, radiomics, computational pathology, multi-omics profiling, and wearable health technologies with advanced AI algorithms has substantially improved the precision and personalization of cancer care across the entire disease continuum. Deep learning, transformer architectures, foundation models, and multimodal AI have demonstrated remarkable capabilities in identifying clinically meaningful biological patterns that extend beyond conventional diagnostic and analytical approaches.

Despite these significant advances, widespread clinical adoption remains dependent on overcoming several important challenges, including limited model interpretability, algorithmic bias, variability in data acquisition, insufficient prospective validation, regulatory complexity, and the need for standardized computational frameworks. Emerging technologies such as explainable AI, federated learning, digital twins, and adaptive multimodal foundation models provide promising solutions that enhance transparency, preserve patient privacy, improve generalizability, and support continuous learning within clinical oncology.

Looking ahead, the future of precision oncology lies in the development of intelligent, continuously learning cancer ecosystems capable of integrating multimodal biological, clinical, and real-world data to deliver personalized prevention, early detection, adaptive treatment, and survivorship care. Achieving this vision

will require rigorous clinical validation, internationally harmonized regulatory standards, ethical governance, robust data-sharing frameworks, and sustained interdisciplinary collaboration among clinicians, computational scientists, engineers, healthcare organizations, patients, and policymakers. Through these collective efforts, AI-enabled digital biomarkers have the potential to redefine cancer care, improve clinical outcomes, reduce healthcare disparities, and establish a new era of personalized and preventive oncology.

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