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Artificial Intelligence–Integrated Cancer Ecosystems: Multimodal Digital Biomarkers for Precision, Personalized, and Preventive Oncology

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ABSTRACT

Artificial intelligence (AI) is reshaping precision oncology by integrating multimodal digital biomarkers—including radiomics, pathomics, genomics, transcriptomics, and liquid biopsy—into unified computational ecosystems that support accurate cancer diagnosis, prognostic stratification, treatment selection, and longitudinal disease monitoring. Recent advances in transformer-based deep learning, vision-language models, self-supervised learning, and foundation models have enabled AI systems to achieve diagnostic performance approaching that of expert radiologists and pathologists while uncovering complex biological patterns beyond conventional analytical methods. Multimodal data fusion further enhances early cancer detection through the simultaneous interpretation of imaging phenotypes, molecular alterations, histopathological features, and clinical variables, facilitating personalized therapeutic decision-making and dynamic digital twin–based disease modeling. Despite these advances, widespread clinical implementation remains constrained by challenges related to model interpretability, algorithmic bias, data privacy, regulatory approval, interoperability, and integration into existing clinical workflows. This review provides a comprehensive overview of AI-integrated cancer ecosystems, highlighting recent developments in deep learning architectures, multimodal digital biomarkers, explainable AI, federated learning, and foundation models. We examine their emerging clinical applications in cancer screening, diagnosis, prognosis, treatment optimization, and response monitoring while discussing ethical, technical, and regulatory considerations for responsible implementation. Current evidence indicates that AI-enabled radiomics and computational pathology are approaching routine clinical deployment as companion diagnostic technologies, whereas privacy-preserving federated learning and multimodal foundation models are expected to accelerate large-scale validation across diverse healthcare systems. Collectively, AI-integrated cancer ecosystems represent a transformative paradigm for precision and preventive oncology, with the potential to improve diagnostic accuracy, personalize cancer management, expand equitable access to advanced analytics, and ultimately enhance patient outcomes worldwide.

Keywords: *Artificial intelligence; precision oncology; digital biomarkers; radiomics; pathomics; genomics; multimodal learning; foundation models; transformer architectures; explainable AI; federated learning; digital twins; computational pathology; preventive oncology.*

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1. Introduction

Cancer remains one of the most biologically heterogeneous diseases, characterized by extensive genomic, epigenomic, transcriptomic, proteomic, metabolic, and microenvironmental diversity that influences tumor initiation, progression, therapeutic response, and clinical outcomes [1]. Conventional clinical classification systems based primarily on histopathology and TNM staging provide valuable prognostic information but fail to fully capture the molecular complexity that underlies individual tumor behavior. Advances in next-generation sequencing, digital pathology, high-resolution imaging, liquid biopsy, and multi-omics technologies have generated unprecedented volumes of multidimensional cancer data.

However, extracting clinically meaningful insights from these complex datasets exceeds the capabilities of traditional statistical and analytical approaches [2].

Artificial intelligence (AI), particularly modern deep learning, has emerged as a transformative computational framework capable of learning hierarchical and nonlinear relationships directly from high-dimensional biomedical data [3]. Unlike conventional rule-based algorithms, deep neural networks automatically discover latent feature representations through iterative optimization, enabling accurate analysis of medical imaging, whole-slide pathology, genomic sequences, electronic health records, and molecular biomarkers. Recent breakthroughs in transformer architectures, self-supervised learning, vision-language models, and large foundation models have further expanded AI's ability to integrate heterogeneous datasets, learn from limited annotations, and generalize across multiple cancer types and clinical settings [4].

These technological advances have driven the emergence of AI-integrated cancer ecosystems—comprehensive computational frameworks that combine radiological imaging, computational pathology, genomics, transcriptomics, proteomics, liquid biopsy, wearable sensor data, and clinical information within interconnected AI pipelines [5]. Rather than functioning as isolated diagnostic algorithms, these ecosystems enable continuous, patient-centered decision support throughout the cancer care continuum, encompassing risk prediction, early detection, molecular characterization, prognostic assessment, therapeutic selection, treatment monitoring, recurrence prediction, and survivorship management. By simultaneously integrating complementary biological information from multiple modalities, AI models can identify complex associations that remain undetectable through single-modality analyses, thereby improving predictive accuracy, clinical interpretability, and personalized treatment planning [6].

Despite remarkable technological progress, translating AI innovations into routine oncology practice remains challenging [7]. Important barriers include limited model explainability, algorithmic bias arising from non-representative training datasets, concerns regarding privacy and cybersecurity, insufficient external validation, interoperability limitations with hospital information systems, and evolving regulatory requirements for AI-based medical devices and companion diagnostics. Ethical considerations—including transparency, accountability, fairness, and equitable access—are equally critical for ensuring responsible clinical implementation.

This review provides a comprehensive overview of AI-integrated cancer ecosystems by examining recent advances in multimodal digital biomarkers, transformer-based deep learning, foundation models, explainable AI, federated learning, and digital twin technologies. We discuss their current and emerging applications in cancer detection, diagnosis, prognostic prediction, treatment optimization, and precision oncology while highlighting the technical, ethical, regulatory, and clinical challenges that must be addressed to enable widespread adoption. Finally, we explore future directions that may accelerate the transition from isolated AI applications toward fully integrated, learning healthcare ecosystems capable of delivering personalized and preventive cancer care on a global scale.

2. Digital Biomarkers in Precision Oncology

Biomarkers have long served as the cornerstone of precision oncology, providing measurable indicators of normal biological processes, disease progression, and therapeutic response [8]. Historically, clinical oncology has relied on single-molecule biomarkers such as prostate-specific antigen (PSA) for prostate cancer screening, HER2 overexpression for breast cancer classification, and microsatellite instability (MSI) for selecting patients likely to benefit from immune checkpoint inhibitors. Although these biomarkers have significantly improved patient management, they capture only limited aspects of the complex biological heterogeneity of cancer and often lack sufficient sensitivity or specificity for individualized therapeutic decision-making.

The emergence of **digital biomarkers** represents a major evolution in biomarker science. Rather than relying on a single laboratory measurement, digital biomarkers integrate quantitative information extracted from medical imaging, computational pathology, genomics, transcriptomics, proteomics, metabolomics, liquid biopsy, and wearable health technologies through advanced AI algorithms [9]. These multidimensional biomarkers provide a comprehensive representation of tumor biology, enabling more accurate characterization of disease behavior. Radiomics converts conventional radiological images into high-dimensional quantitative descriptors that reflect tumor heterogeneity, morphology, and microenvironmental characteristics [10]. Similarly, pathomics extracts detailed morphological, architectural, and cellular features from whole-slide histopathology images that frequently extend beyond the limits of visual interpretation by expert pathologists [11]. Multi-omics integration further combines genomic, transcriptomic, proteomic, and metabolomic information to identify oncogenic pathways, therapeutic vulnerabilities, and mechanisms of drug resistance [12]. In parallel, liquid biopsy technologies—including circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), exosomal biomarkers, and circulating proteins—offer minimally invasive approaches for longitudinal disease monitoring, treatment response assessment, and early detection of recurrence [8].

Artificial intelligence has become the enabling technology that transforms these complex datasets into clinically actionable digital biomarkers [13]. Deep learning models trained on large, annotated datasets automatically learn intricate relationships between imaging, molecular, and pathological features that correlate with diagnosis, prognosis, and treatment response. For instance, AI-based analysis of breast cancer histopathology can simultaneously quantify tumor-infiltrating lymphocytes, stromal composition, nuclear atypia, glandular architecture, and spatial cellular organization, generating integrated biomarkers capable of predicting response to neoadjuvant chemotherapy and long-term recurrence risk [14]. Likewise, radiomics

models identify subtle variations in tumor texture, shape, intensity, and spatial heterogeneity that correlate with genomic alterations, therapeutic sensitivity, and overall survival beyond conventional radiological interpretation [15].

Collectively, AI-driven digital biomarkers have shifted oncology from population-based risk estimation toward truly individualized cancer management. Instead of assigning patients to broad prognostic categories based solely on demographic characteristics, tumor stage, or histological grade, multimodal AI models generate personalized predictions regarding recurrence risk, therapeutic response, survival probability, and optimal treatment strategies for each individual patient, thereby advancing the realization of precision oncology [5].

3. Artificial Intelligence and Computational Oncology

Artificial intelligence has become a central computational framework in modern oncology, with deep learning driving major advances in cancer detection, diagnosis, prognosis, and treatment prediction [7]. Convolutional neural networks (CNNs) established the foundation for AI-powered medical image analysis by learning hierarchical feature representations directly from imaging data. Through successive convolutional layers, CNNs progressively identify low-level visual features such as edges and textures, intermediate structural patterns, and ultimately complex pathological characteristics associated with specific tumor types [3]. Transfer learning, in which CNNs pretrained on large image repositories such as ImageNet are subsequently fine-tuned using cancer-specific datasets, has substantially improved diagnostic performance while reducing the need for extensive annotated medical imaging collections [4].

More recently, Vision Transformers (ViTs) have emerged as a powerful alternative to CNNs for computational pathology and medical imaging [16]. Unlike convolution-based architectures that primarily analyze local neighborhoods, ViTs employ self-attention mechanisms capable of modeling long-range spatial relationships across entire images. This global contextual understanding is particularly advantageous for analyzing gigapixel whole-slide pathology images, where interactions between distant tissue regions may contain diagnostically important information regarding tumor architecture, stromal organization, and immune infiltration [17]. Furthermore, foundation models pretrained on millions of unlabeled pathology images develop highly transferable feature representations that can be efficiently adapted to diverse downstream oncology applications using relatively small labeled datasets [18].

Large language models (LLMs) have further expanded AI capabilities by enabling comprehensive analysis of unstructured clinical information, including pathology reports, radiology narratives, genomic reports, multidisciplinary tumor board discussions, and electronic health records [19]. Transformer-based LLMs learn contextual semantic representations of medical language, facilitating extraction of clinically relevant information and supporting automated clinical documentation. When integrated with vision-based AI systems, multimodal architectures can simultaneously analyze radiological images, histopathology slides, genomic findings, and clinical narratives to generate unified patient-specific tumor profiles and comprehensive decision-support recommendations [20].

Self-supervised learning has emerged as another transformative paradigm that addresses one of oncology AI's greatest limitations—the scarcity of expertly annotated datasets [16]. Rather than relying exclusively on manually labeled images, self-supervised models learn meaningful feature representations from large collections of unlabeled medical data using surrogate learning objectives such as masked image reconstruction and contrastive learning. Foundation models including UNI and CONCH, trained through self-supervised learning on massive pathology image repositories, have demonstrated exceptional transfer learning performance across numerous cancer-related classification, segmentation, and prognostic prediction tasks while requiring minimal task-specific annotation [21].

Together, these advances in deep learning architectures, transformer models, multimodal learning, and self-supervised foundation models have established computational oncology as a rapidly evolving discipline capable of integrating heterogeneous biomedical data into clinically meaningful insights, thereby supporting increasingly personalized cancer care.

4. Concept of AI-Integrated Cancer Ecosystems

AI-integrated cancer ecosystems represent a comprehensive transformation of oncology from fragmented, specialty-specific workflows toward unified, patient-centered computational platforms that integrate diverse biomedical information throughout the entire cancer care continuum [1]. Instead of treating radiological imaging, pathology, genomics, laboratory biomarkers, and clinical information as independent sources of evidence, these ecosystems combine them into interconnected analytical frameworks that support diagnosis, prognostic assessment, treatment selection, and continuous disease monitoring.

The architecture of an AI-integrated cancer ecosystem typically consists of four interconnected components: **data integration, multimodal analytics, clinical decision support, and continuous outcome monitoring** [6]. The data integration layer aggregates heterogeneous information from radiological imaging modalities such as CT, MRI, PET, and ultrasound; digital pathology whole-slide images; genomic and multi-omics sequencing; liquid biopsy assays; wearable sensor technologies; electronic health records; and longitudinal treatment histories into standardized, interoperable datasets [22]. The multimodal analytics layer employs advanced AI algorithms to identify relationships among imaging phenotypes, molecular alterations, pathological architecture, immune microenvironment characteristics, and clinical variables that collectively determine tumor behavior. Clinical decision-support systems subsequently translate these predictions into evidence-based recommendations while incorporating explainable AI methods that improve transparency and clinician confidence. Finally, continuous outcome monitoring captures longitudinal information regarding treatment response, disease progression, toxicity, recurrence, and survival, allowing AI models to undergo ongoing recalibration and performance improvement.

Within clinical practice, AI-integrated cancer ecosystems provide four major functional capabilities. First, **precision diagnosis** combines multimodal information to improve tumor classification, molecular subtyping, and disease staging beyond the capabilities of individual diagnostic modalities [23]. Second, **prognostic stratification** integrates imaging, molecular, and pathological biomarkers to generate individualized predictions of recurrence, metastasis, and overall survival, thereby supporting personalized surveillance strategies and early intervention [24]. Third, **predictive therapeutics** utilizes genomic alterations, transcriptomic signatures, radiomic characteristics, and pathological features to estimate the likelihood of response to chemotherapy, targeted therapy, immunotherapy, or combination treatment, enabling more effective treatment selection while minimizing unnecessary toxicity [23]. Finally, **preventive oncology** identifies individuals at elevated cancer risk by integrating inherited genetic susceptibility, imaging biomarkers, longitudinal biomarker trajectories, and lifestyle-related data, facilitating early detection and preventive interventions before clinically overt disease develops [25].

The principal advantage of AI-integrated cancer ecosystems lies in their ability to capture the multidimensional nature of cancer biology. Molecular alterations influence imaging characteristics, histopathological architecture reflects genomic and transcriptomic changes, immune microenvironment composition affects therapeutic response, and clinical outcomes emerge from complex interactions among these interconnected biological processes. By simultaneously analyzing these complementary sources of information rather than evaluating each independently, AI-integrated cancer ecosystems achieve superior predictive performance, generate more biologically meaningful insights, and provide a robust foundation for precision and preventive oncology in routine clinical practice [6].

5. Digital Biomarkers in Precision Oncology

Digital biomarkers derived from radiological imaging, computational pathology, molecular profiling, and liquid biopsy have emerged as essential components of precision oncology by providing quantitative, reproducible measures that predict clinically relevant outcomes such as diagnosis, therapeutic response, disease progression, and survival [8]. Unlike conventional biomarkers that categorize patients into broad risk groups, AI-enabled digital biomarkers generate individualized predictions that reflect the unique biological characteristics of each patient's tumor, thereby facilitating personalized clinical decision-making [14].

Growing clinical evidence supports the utility of digital biomarkers across multiple cancer types. In a multicenter study involving 1,035 patients with breast cancer, deep learning–derived histopathological biomarkers based on tumor epithelial architecture and stromal composition significantly improved prediction of response to neoadjuvant therapy when combined with conventional clinical variables [10]. The integration of AI-derived image features with immune profiling achieved an area under the receiver operating characteristic curve (AUC) of 0.831 compared with 0.706 using clinicopathological variables alone, demonstrating a substantial improvement in predictive performance and supporting more individualized treatment planning [10]. Similarly, in pancreatic ductal adenocarcinoma, AI-powered computational pathology identified prognostically important immune and stromal characteristics, including increased macrophage infiltration and elevated stromal entropy, both of which were associated with poorer survival and differential response to neoadjuvant therapy—features that are difficult to quantify reliably through routine microscopic examination [11].

Digital biomarkers also enable continuous, minimally invasive disease monitoring throughout the cancer treatment pathway [8]. Unlike repeated tissue biopsies, which are invasive, expensive, and impractical for serial assessment, longitudinal radiomic analysis of computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) provides quantitative evaluation of temporal changes in tumor burden, heterogeneity, and treatment response [6]. Liquid biopsy technologies, particularly circulating tumor DNA (ctDNA), facilitate early detection of minimal residual disease and molecular relapse several weeks or months before recurrence becomes radiologically apparent, thereby creating opportunities for earlier therapeutic intervention [8]. Integrating serial imaging biomarkers with ctDNA dynamics enables comprehensive monitoring of disease evolution and supports adaptive treatment strategies tailored to changing tumor biology.

An important application of digital biomarkers is the non-invasive characterization of molecular tumor subtypes and prediction of immunotherapy responsiveness [26]. Patients with non-small-cell lung cancer (NSCLC) who share identical histological classification and TNM stage often exhibit markedly different responses to immune checkpoint inhibitors because of underlying molecular and immunological heterogeneity. AI-based radiomics has demonstrated the ability to identify imaging signatures associated with clinically important genomic alterations such as EGFR mutations, KRAS mutations, ALK rearrangements, tumor mutational burden, and immune microenvironment characteristics, allowing non-invasive molecular profiling without repeated tissue sampling [27]. Comparable approaches have also been successfully applied in breast cancer, where deep learning analysis of magnetic resonance imaging predicts hormone receptor status, HER2 expression, and proliferative activity, thereby supporting personalized therapeutic planning while reducing reliance on additional invasive diagnostic procedures [15].

Collectively, digital biomarkers represent a paradigm shift in oncology by integrating multimodal biological information into clinically actionable AI models capable of improving diagnosis, therapeutic selection, disease surveillance, and long-term patient management.

6. Radiomics and Imaging Biomarkers

Radiomics has transformed medical imaging from a predominantly qualitative discipline into a quantitative science by systematically extracting large numbers of computational imaging features from routine radiological examinations [15]. Through automated analysis of CT, MRI, PET, and ultrasound images, radiomics quantifies tumor morphology, texture, intensity, shape, and spatial heterogeneity, providing objective biomarkers that complement conventional radiological interpretation and improve clinical decision-making [28].

The standard radiomics workflow consists of four major stages: image acquisition, lesion segmentation, quantitative feature extraction, and predictive model development [28]. Following image acquisition, tumors are segmented either manually, semi-automatically, or fully automatically to define regions of interest. Quantitative imaging features are subsequently extracted to characterize tumor geometry, internal texture, signal intensity, and spatial organization before being incorporated into statistical or machine learning models that predict clinically meaningful outcomes.

Traditional radiomic features can be broadly categorized into morphological descriptors—including tumor volume, surface area, compactness, and shape irregularity—and texture descriptors that quantify intratumoral heterogeneity using methods such as gray-level co-occurrence matrices, gray-level run-length matrices, and entropy analysis [29]. These handcrafted features capture biologically relevant imaging characteristics that often correlate with tumor aggressiveness, vascularity, cellularity, and treatment response. Nevertheless, handcrafted radiomic descriptors remain inherently constrained because they rely on predefined mathematical formulations that may overlook subtle imaging patterns associated with complex tumor biology [30].

Deep learning has substantially expanded the capabilities of radiomics by enabling automatic feature learning directly from imaging data without requiring manual feature engineering [29]. Convolutional neural networks (CNNs) progressively learn hierarchical imaging representations, beginning with low-level features such as edges, gradients, and textures before developing increasingly abstract representations associated with tumor architecture, biological heterogeneity, and clinical outcomes. Studies have consistently demonstrated that deep radiomic features outperform conventional handcrafted radiomics for numerous diagnostic and prognostic applications [15]. Hybrid models that combine handcrafted radiomic features with CNN-derived deep features frequently provide the highest predictive accuracy by integrating biological interpretability with advanced pattern-recognition capabilities [28].

Radiomics has demonstrated significant clinical value across diverse malignancies. In early-stage lung cancer, CT-based radiomic signatures predict clinically actionable molecular alterations, including EGFR mutations and ALK rearrangements, thereby facilitating selection of targeted therapies without repeated invasive biopsies [27]. In glioblastoma, MRI-derived radiomic biomarkers accurately predict MGMT promoter methylation status, an important determinant of responsiveness to temozolomide chemotherapy, allowing non-invasive treatment stratification [31]. In breast cancer, deep learning–enhanced radiomics distinguishes luminal A and luminal B molecular subtypes on dynamic contrast-enhanced MRI with reported AUC values approaching 0.92, improving prognostic assessment and treatment planning [15]. Similarly, radiomic biomarkers in pancreatic cancer have been associated with overall survival, metastatic potential, and therapeutic response, enabling more precise risk stratification and individualized follow-up strategies [29].

Despite these encouraging advances, several challenges continue to limit widespread clinical implementation of radiomics [32]. Quantitative imaging features are often influenced by scanner manufacturers, acquisition protocols, image reconstruction techniques, segmentation variability, and preprocessing methods, resulting in reduced reproducibility across institutions. Furthermore, most published radiomics studies remain retrospective and single-center, limiting external generalizability. Future progress will depend on standardized imaging protocols, harmonized feature extraction methodologies, prospective multicenter validation, and integration with explainable AI frameworks to facilitate regulatory approval and routine adoption within clinical oncology practice [27].

7. Pathomics and Computational Histopathology

Computational histopathology, commonly referred to as pathomics, applies artificial intelligence (AI) to digitized histopathological images to extract quantitative biomarkers from tissue architecture, cellular morphology, and spatial organization [7]. Unlike radiomics, which analyzes radiological images acquired for diagnostic purposes, pathomics utilizes routinely prepared histopathology slides, allowing AI-based analysis to be integrated into existing pathology workflows without requiring additional patient investigations.

The widespread adoption of whole-slide imaging (WSI) has facilitated the development of computational pathology by enabling the digitization of glass slides into gigapixel-resolution images suitable for AI analysis [4]. A single whole-slide image contains millions to billions of pixels and encompasses thousands of microscopic fields, creating datasets far beyond the capacity of manual interpretation alone. Deep learning algorithms can automatically segment tissue compartments, classify tumor and stromal regions, identify individual cell populations, quantify immune infiltration, evaluate nuclear morphology, and analyze spatial relationships among tumor cells and the surrounding microenvironment [11]. These quantitative analyses provide objective measurements that complement conventional pathological assessment while reducing observer variability.

Pathomics has demonstrated considerable clinical value in predicting prognosis and therapeutic response across multiple malignancies. In a multicenter study involving 603 patients with breast cancer, self-supervised vision

transformers integrated whole-slide histopathology images with clinical variables to infer transcriptomic profiles, achieving an area under the receiver operating characteristic curve (AUC) of 0.929 for predicting pathological complete response following neoadjuvant therapy [33]. This performance significantly exceeded conventional clinicopathological models (AUC 0.815) and remained robust during external validation across independent patient cohorts [33]. Similar AI-based computational pathology approaches have successfully predicted recurrence risk, hormone receptor status, HER2 expression, Ki-67 proliferation index, and molecular subtypes directly from hematoxylin and eosin (H&E)-stained slides, thereby reducing dependence on additional immunohistochemical testing [4].

Recent advances in foundation models have further accelerated progress in computational pathology. Large-scale self-supervised models pretrained on hundreds of millions of pathology image patches learn generalized tissue representations that can be transferred efficiently to numerous downstream diagnostic and prognostic tasks [18]. For example, the Prov-GigaPath foundation model, trained on approximately 1.3 billion pathology image patches derived from 171,189 whole-slide images, achieved state-of-the-art performance across 25 of 26 benchmarked cancer classification and pathomics tasks [18]. Such pretrained models substantially reduce the need for extensive annotated datasets and enable rapid development of specialized AI systems for specific clinical applications.

Interpretability remains particularly important in computational pathology because diagnostic decision-making traditionally relies on visual recognition of morphological patterns by expert pathologists [34]. Consequently, AI systems must provide not only high diagnostic accuracy but also transparent reasoning that aligns with established pathological principles. Explainable AI techniques—including attention maps, Gradient-weighted Class Activation Mapping (Grad-CAM), integrated gradients, and attention-based visualization—highlight image regions contributing most strongly to model predictions, thereby improving clinician confidence, facilitating validation of AI outputs, and promoting responsible clinical implementation [35].

Overall, computational histopathology represents one of the most mature applications of AI in oncology, enabling objective tissue characterization, improved prognostic assessment, enhanced treatment prediction, and scalable precision pathology for routine clinical practice.

8. Genomics, Multi-Omics, and Liquid Biopsy Integration

Genomic profiling has become an essential component of precision oncology by identifying molecular alterations that influence tumor behavior, therapeutic susceptibility, and mechanisms of drug resistance [36]. Next-generation sequencing (NGS) enables comprehensive analysis of thousands of genes simultaneously, facilitating identification of clinically actionable genomic alterations such as EGFR mutations, ALK rearrangements, BRAF mutations, BRCA alterations, microsatellite instability (MSI), and high tumor mutational burden (TMB). These biomarkers guide the selection of targeted therapies and immunotherapeutic agents. Nevertheless, genomic alterations alone frequently fail to explain the full spectrum of treatment response, as patients harboring identical driver mutations often demonstrate considerable biological and clinical heterogeneity.

To address these limitations, multi-omics integration combines genomic information with complementary molecular datasets, including transcriptomics (gene expression), proteomics (protein abundance), epigenomics (DNA methylation and histone modifications), metabolomics (metabolic profiling), and other molecular layers to generate a comprehensive representation of tumor biology [1]. Integrating these heterogeneous data sources requires sophisticated computational approaches because each modality differs substantially in dimensionality, scale, and biological interpretation. Early integration strategies concatenate all molecular features into a single dataset before model training but may allow dominant data modalities to obscure weaker biological signals. Late integration approaches develop independent predictive models for each modality before combining their outputs, although they may fail to capture complex interactions among biological systems. More advanced intermediate integration methods—including graph neural networks, multimodal transformers, and attention-based fusion architectures—explicitly model relationships across multiple molecular modalities, thereby improving biological interpretability and predictive performance [1].

AI-powered multi-omics integration has demonstrated remarkable potential for improving cancer diagnosis and prognosis. In gastric cancer, the integration of exon expression, messenger RNA (mRNA), microRNA (miRNA), and DNA methylation profiles using multiple-instance learning and ensemble machine learning achieved a classification accuracy of 98.1%, substantially outperforming models based on individual omics datasets [37]. Likewise, multimodal integration of genomic sequencing data with radiomic imaging features for lung cancer mutation prediction achieved an AUC of 0.963, exceeding the predictive performance of imaging-only (AUC 0.917) and genomics-only (AUC 0.893) models, highlighting the complementary biological information contributed by each modality [27].

Liquid biopsy technologies have emerged as an important extension of precision oncology by enabling minimally invasive, real-time monitoring of tumor evolution through circulating biomarkers [8]. Circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), exosomes, and circulating proteins provide dynamic molecular information that reflects tumor burden, treatment response, and clonal evolution without the need for repeated tissue biopsies. Detection of ctDNA enables identification of minimal residual disease and molecular relapse several weeks or months before recurrence becomes detectable by conventional imaging, thereby creating opportunities for earlier therapeutic intervention. Integration of serial ctDNA measurements

with radiomic biomarkers, clinical variables, and treatment history facilitates the construction of digital twin models capable of predicting disease progression and treatment response over time [6]. For example, in patients with ALK-rearranged non-small-cell lung cancer, machine learning models integrating volumetric imaging features, longitudinal ctDNA measurements, and clinical characteristics accurately predicted progression-free survival and identified patients most likely to benefit from treatment intensification during prospective clinical evaluation [6].

Despite its considerable promise, implementation of multi-omics integration remains technically challenging. Clinical datasets frequently contain incomplete molecular profiles, heterogeneous sequencing platforms introduce batch effects, and the high dimensionality of omics data requires substantial computational infrastructure. Furthermore, multicenter collaboration is often constrained by privacy regulations governing patient data sharing. Emerging federated learning frameworks provide a promising solution by enabling collaborative AI model development across multiple institutions while maintaining data locally, thereby improving model generalizability, preserving patient privacy, and accelerating the clinical translation of AI-enabled multi-omics precision oncology [38].

9. Deep Learning, Foundation Models, and Transformer Architectures in Oncology

Deep learning has revolutionized computational oncology, with transformer architectures emerging as one of the most influential developments in artificial intelligence owing to their exceptional ability to capture long-range dependencies, integrate heterogeneous information, and generalize across diverse clinical tasks [39]. Unlike convolutional neural networks (CNNs), which primarily analyze local image neighborhoods through convolutional operations, transformers employ self-attention mechanisms that allow every element of the input to interact directly with every other element. This global receptive field enables transformers to capture complex spatial and contextual relationships that are particularly valuable for understanding heterogeneous tumor biology.

In medical imaging, Vision Transformers (ViTs) divide images into small patches that are subsequently processed through multiple transformer encoder layers equipped with multi-head self-attention mechanisms [40]. Each attention head learns complementary information by focusing on different image characteristics, such as tumor margins, internal heterogeneity, vascular architecture, or surrounding stromal tissues. This parallel attention mechanism generates richer and more informative feature representations than conventional convolutional approaches. Furthermore, Vision Transformers have demonstrated greater robustness to variations in imaging protocols, scanner manufacturers, and acquisition parameters, thereby improving generalizability across different healthcare institutions and enhancing their suitability for clinical deployment [41].

Applying transformer architectures to computational pathology presents unique computational challenges because whole-slide images contain billions of pixels and thousands of image patches. Processing every image patch simultaneously using global attention is computationally prohibitive. To overcome this limitation, hierarchical Vision Transformers process pathology images at multiple spatial resolutions by first analyzing local tissue regions before integrating information across larger tissue structures [42]. This hierarchical strategy preserves both local cellular detail and global tissue architecture while maintaining computational efficiency. Additionally, foundation models pretrained through self-supervised learning on hundreds of millions of pathology image patches acquire generalized tissue representations that can be efficiently transferred to numerous downstream pathology tasks with minimal annotated data [16].

Large language models (LLMs) have further expanded the role of AI in oncology by enabling comprehensive analysis of unstructured clinical narratives, including pathology reports, radiology interpretations, multidisciplinary tumor board documentation, genomic reports, and electronic health records [19]. Transformer-based language models learn contextual semantic representations that capture complex clinical relationships embedded within medical text [43]. When integrated with vision-based AI systems, multimodal architectures simultaneously analyze imaging findings, histopathological features, molecular alterations, and clinical documentation to generate unified patient-specific representations that support diagnosis, prognostic assessment, and therapeutic decision-making [20].

Self-supervised learning has emerged as another transformative advancement by addressing the limited availability of expert-labeled medical datasets [16]. Instead of relying exclusively on manually annotated images, self-supervised approaches learn meaningful representations from large collections of unlabeled data using surrogate tasks such as masked image reconstruction and contrastive learning. Foundation models including UNI and CONCH, pretrained on more than 40 million pathology image patches, have demonstrated exceptional transfer learning capabilities, achieving high diagnostic accuracy across numerous downstream oncology applications using relatively small labeled datasets [21]. These models substantially reduce development costs, improve scalability, and democratize AI adoption for institutions with limited annotation resources.

Collectively, transformer architectures, foundation models, and self-supervised learning are redefining computational oncology by enabling scalable, data-efficient, and highly generalizable AI systems capable of supporting precision cancer diagnosis and personalized treatment planning.

10. Multimodal AI Fusion Strategies

Multimodal artificial intelligence represents a fundamental advancement in precision oncology by integrating heterogeneous data sources—including radiological imaging, computational pathology, genomics, multi-omics, electronic health records,

laboratory biomarkers, and wearable sensor data—into unified predictive models [20]. Rather than analyzing each modality independently, multimodal AI explicitly models the complex biological interactions that exist among different sources of patient information, thereby improving diagnostic accuracy and clinical decision-making.

Several computational strategies have been developed for multimodal data integration. Early fusion combines features from all modalities into a single unified feature representation before model training, enabling direct interaction among heterogeneous data types but often making models sensitive to missing data and dominant feature modalities [44]. Late fusion independently analyzes each modality using separate AI models before combining their predictions through ensemble learning or meta-classification approaches. Although this strategy provides greater flexibility when individual modalities are unavailable, it may overlook important biological interactions among different data sources.

To overcome these limitations, more sophisticated intermediate fusion approaches employ co-attention mechanisms that explicitly learn relationships among multiple modalities. In pathology-radiology integration, for example, co-attention enables histopathological features to guide interpretation of radiological findings while simultaneously allowing imaging characteristics to influence pathological feature weighting, thereby generating biologically meaningful multimodal representations [45].

Graph neural networks (GNNs) provide another powerful framework for multimodal fusion by representing diverse biological entities as interconnected graph structures [44]. Imaging biomarkers, pathological features, genomic alterations, immune cell populations, and clinical variables are represented as graph nodes, whereas biological or spatial relationships are represented as graph edges. Through iterative message passing, graph convolutional networks learn complex interactions among these interconnected biological components. This approach is particularly valuable for modeling the tumor microenvironment, where interactions among immune cells, stromal elements, vascular structures, and malignant cells collectively influence therapeutic response and disease progression [46].

More recently, transformer-based multimodal fusion has emerged as one of the most effective strategies for integrating heterogeneous biomedical data [20]. Separate encoders first transform each modality into latent feature embeddings, after which cross-modal attention mechanisms learn interactions among imaging, pathology, genomics, and clinical information. Cross-attention enables AI models to identify relationships such as imaging features associated with specific genomic mutations or pathological characteristics predictive of treatment response. Importantly, transformer-based architectures naturally accommodate incomplete clinical datasets because missing modalities can simply be represented by absent embeddings without requiring complete retraining of the model.

Numerous studies have demonstrated the clinical superiority of multimodal AI over single-modality approaches. Integration of radiological imaging and computational pathology for breast cancer molecular subtyping achieved an AUC of 0.929, significantly outperforming imaging-only (AUC 0.815) and pathology-only (AUC 0.802) models [33]. Similarly, combining radiomic imaging with genomic sequencing improved lung cancer mutation prediction from an AUC of 0.917 using imaging alone to 0.963 using multimodal integration [27]. In pancreatic cancer, multimodal fusion incorporating imaging, pathology, genomics, and clinical variables significantly enhanced patient stratification, prognostic prediction, and therapeutic response assessment compared with single-modality AI systems [45].

Overall, multimodal AI fusion constitutes the computational foundation of next-generation precision oncology by enabling comprehensive interpretation of complex biological information and supporting more accurate, individualized clinical decision-making.

11. Applications of AI-Integrated Cancer Ecosystems

11.1 Early Cancer Detection

Early cancer detection remains one of the most impactful applications of AI-integrated cancer ecosystems because diagnosis at localized stages substantially improves treatment success, long-term survival, and overall patient outcomes [25]. AI-powered screening platforms combine radiological imaging, digital biomarkers, molecular profiling, and individualized risk prediction to distinguish clinically significant malignancies from benign or indolent lesions while reducing unnecessary diagnostic procedures.

In breast cancer screening, AI-enhanced mammography has demonstrated considerable improvements in diagnostic performance. Deep learning models based on convolutional neural networks and Vision Transformers accurately identify mammographic abnormalities with sensitivity and specificity comparable to—or exceeding—that of experienced radiologists, particularly in women with dense breast tissue or subtle imaging findings that are difficult to detect through conventional interpretation [47]. Furthermore, integrating mammographic imaging with additional risk factors, including polygenic risk scores, breast density, family history, and previous imaging findings, enables personalized risk-based screening strategies that outperform traditional population-based screening recommendations [3].

In lung cancer, AI-assisted analysis of low-dose computed tomography (LDCT) has shown substantial promise for identifying pulmonary nodules requiring immediate intervention while reducing false-positive findings that often result in unnecessary biopsies and patient anxiety [41]. Deep learning algorithms integrate nodule size, morphology, texture, growth characteristics, and patient-specific clinical variables such as smoking history and prior imaging examinations to improve diagnostic accuracy. Advanced radiomic models additionally predict clinically relevant molecular

alterations—including EGFR, KRAS, and ALK mutations—from imaging alone, enabling non-invasive molecular characterization before tissue biopsy and supporting earlier selection of targeted therapies [27].

AI has also transformed colorectal cancer screening through intelligent endoscopic image analysis. Deep learning–assisted colonoscopy systems accurately identify adenomatous and dysplastic polyps in real time, achieving near-expert detection sensitivity while reducing missed lesions during routine examinations [48]. When combined with fecal biomarkers, genetic susceptibility profiles, and patient-specific clinical characteristics, multimodal AI models enable personalized colorectal cancer screening strategies in which individuals at elevated risk undergo intensified surveillance, whereas lower-risk individuals continue with standard screening intervals. Such risk-adapted approaches improve early detection while optimizing healthcare resource utilization.

Across multiple cancer types, AI-integrated early detection systems are shifting oncology from reactive diagnosis toward proactive cancer prevention by enabling earlier identification of biologically significant disease, individualized screening recommendations, and timely therapeutic intervention, thereby laying the foundation for more effective precision and preventive oncology.

12. Cancer Risk Prediction

Cancer risk prediction is a cornerstone of preventive oncology, enabling the identification of individuals at increased risk of developing malignancy before the onset of clinical disease [25]. AI-integrated cancer ecosystems combine inherited genetic susceptibility, imaging biomarkers, laboratory parameters, environmental exposures, lifestyle factors, and clinical history to generate individualized risk estimates that support preventive interventions, personalized screening strategies, and early surveillance.

In hereditary breast cancer, AI models integrating BRCA1/BRCA2 mutations, polygenic risk scores, mammographic characteristics, breast density, and demographic variables have demonstrated significantly greater predictive accuracy than conventional clinical risk assessment models [3]. Polygenic risk scores provide complementary information to imaging biomarkers, allowing AI systems to generate more comprehensive and individualized estimates of future cancer risk [25]. Similar multimodal approaches have been applied to pancreatic cancer by integrating germline mutations in DNA repair genes, including BRCA2, radiological features such as pancreatic cystic lesions and glandular atrophy, and circulating biomarkers to identify high-risk individuals who may benefit from intensified surveillance using advanced imaging or endoscopic evaluation [25].

In colorectal cancer, AI-based predictive models integrate family history, hereditary cancer syndromes, germline genetic variants, imaging findings, and molecular biomarkers to estimate the likelihood that colorectal polyps contain advanced dysplasia or malignant transformation. Such individualized risk stratification supports personalized surveillance intervals, optimized colonoscopy scheduling, and earlier intervention for high-risk patients while reducing unnecessary procedures in lower-risk populations [3].

Overall, AI-driven cancer risk prediction facilitates a transition from population-based screening toward personalized preventive oncology by enabling proactive identification of individuals most likely to benefit from targeted surveillance and risk-reduction strategies.

13. Tumor Classification

Accurate tumor classification is fundamental to precision oncology because histological subtype, molecular characteristics, and tumor grade directly influence prognosis, therapeutic selection, and clinical outcomes [49]. AI-integrated cancer ecosystems improve tumor classification by simultaneously analyzing radiological imaging, computational pathology, genomic alterations, and clinical information, thereby achieving greater diagnostic accuracy than single-modality approaches.

In gastric cancer, deep learning models integrating endoscopic ultrasound, histopathology, and genomic profiling accurately classify tumors according to both Laurén histological subtypes (intestinal, diffuse, and mixed) and molecular classifications, including microsatellite instability (MSI), chromosomal instability, genomic stability, and Epstein–Barr virus (EBV)-associated disease [49]. These classifications have substantial clinical importance because diffuse-type gastric cancers generally demonstrate poorer prognosis and different therapeutic responses compared with intestinal-type tumors, whereas MSI-high tumors frequently respond favorably to immune checkpoint inhibitors irrespective of other clinicopathological characteristics.

Glioma represents another important application of multimodal AI classification. Integration of magnetic resonance imaging (MRI), histopathological findings, and molecular biomarkers—including IDH mutation status, 1p/19q codeletion, and MGMT promoter methylation—enables accurate classification into biologically and prognostically distinct subgroups [30]. Deep learning–based radiomics has demonstrated the ability to predict IDH mutation status and 1p/19q codeletion directly from preoperative MRI, providing non-invasive molecular characterization that may reduce reliance on invasive biopsy procedures [28].

Similarly, in lymphoma, multimodal AI systems integrating positron emission tomography (PET), histopathological assessment, flow cytometry, immunophenotyping, and genomic profiling improve classification of lymphoma subtypes and facilitate more accurate prognostic stratification, thereby supporting individualized therapeutic planning [49].

By integrating complementary biological information from multiple diagnostic modalities, AI-integrated tumor classification provides a more comprehensive understanding of tumor biology and enables increasingly precise, personalized cancer management.

14. Prognostic Prediction

Accurate prognostic prediction enables clinicians to estimate an individual patient's risk of recurrence, distant metastasis, disease progression, and overall survival, thereby guiding treatment intensity, follow-up strategies, and long-term clinical management [24]. AI-integrated cancer ecosystems combine radiological, pathological, genomic, molecular, and clinical data to generate individualized prognostic models that consistently outperform conventional statistical nomograms.

In breast cancer, multimodal deep learning models integrating computational pathology, clinical variables, and immune microenvironment characteristics have demonstrated significant improvements in predicting distant recurrence-free survival [14]. Self-supervised Vision Transformer models analyzing whole-slide histopathology images together with clinical information achieved a concordance index (C-index) of 0.698 for predicting distant recurrence-free interval within The Cancer Genome Atlas (TCGA) cohort, outperforming traditional clinicopathological prognostic models [50]. Importantly, these AI systems also incorporate explainable AI techniques that identify pathological features responsible for prognostic predictions, thereby improving clinician confidence and interpretability.

In prostate cancer, integration of multiparametric magnetic resonance imaging (mpMRI) with genomic profiling enables accurate non-invasive risk stratification for clinically significant disease [51]. Radiomic biomarkers extracted from mpMRI accurately predict biopsy outcomes, molecular alterations, and tumor aggressiveness, supporting decisions regarding active surveillance, focal therapy, or definitive treatment while reducing unnecessary invasive procedures [51].

In patients with ALK-rearranged non-small-cell lung cancer, AI models combining volumetric imaging changes, serial circulating tumor DNA (ctDNA) measurements, and demographic characteristics have demonstrated excellent prognostic performance in prospective clinical studies [6]. These models identify patients at high risk of progression despite first-generation tyrosine kinase inhibitors (TKIs), allowing earlier transition to second-generation targeted therapies before radiological progression becomes clinically apparent.

Overall, AI-driven prognostic prediction enables individualized outcome estimation and supports more precise therapeutic decision-making throughout the continuum of cancer care.

15. Precision Therapeutics

Precision therapeutics aims to match each patient with the treatment strategy most likely to achieve durable clinical benefit while minimizing unnecessary toxicity and ineffective interventions [8]. AI-integrated cancer ecosystems combine genomic alterations, radiomic imaging features, computational pathology, molecular biomarkers, and longitudinal treatment data to predict therapeutic response and optimize individualized treatment selection.

In lung cancer, AI models integrating genomic driver mutations with imaging characteristics, pathological findings, and clinical variables facilitate selection among chemotherapy, targeted therapy, and immunotherapy [27]. Tumors harboring EGFR mutations demonstrate preferential responses to EGFR tyrosine kinase inhibitors, ALK-rearranged tumors respond to ALK inhibitors, whereas tumors characterized by elevated PD-L1 expression and high tumor mutational burden (TMB) are more likely to benefit from immune checkpoint blockade. By simultaneously analyzing molecular and imaging biomarkers, AI systems improve prediction of therapeutic efficacy while identifying patients at increased risk of developing acquired resistance mutations that may require early modification of treatment strategies [27].

In gastric cancer, multimodal AI models integrating histopathological subtype, radiological imaging, and molecular biomarkers accurately predict response to 5-fluorouracil-based neoadjuvant chemotherapy [49]. For example, tumors classified as the basal-like subtype according to the Moffitt classification generally exhibit poor responsiveness to standard chemotherapy. Early identification of these tumors through AI-guided analysis enables clinicians to consider alternative treatment strategies, enrollment in clinical trials, or personalized therapeutic approaches before treatment initiation [49].

Emerging approaches combining patient-derived three-dimensional tumor models with AI-driven drug prioritization represent a promising frontier in precision oncology [23]. AI algorithms analyze tumor genomics, histopathological characteristics, and molecular signatures to predict candidate therapeutic agents, which are subsequently evaluated using patient-specific organoid or three-dimensional tumor models. This integrated computational and experimental workflow enables individualized drug sensitivity testing, facilitating selection of therapies with the highest likelihood of clinical success while reducing exposure to ineffective treatments.

Collectively, AI-integrated precision therapeutics is transforming oncology from standardized treatment algorithms toward highly personalized therapeutic strategies based on each patient's unique tumor biology, thereby improving treatment efficacy, minimizing toxicity, and advancing the goals of precision medicine.

16. Immuno-Oncology

Immunotherapy has transformed cancer treatment by harnessing the host immune system to eliminate malignant cells. However, therapeutic response varies considerably among patients because of the complex interactions between tumor biology, the immune microenvironment, and host immune competence [26]. AI-integrated cancer ecosystems provide a comprehensive framework for characterizing these interactions by combining radiological imaging, computational pathology, genomic profiling, and circulating biomarkers to predict immunotherapy response, identify mechanisms of resistance, and support individualized treatment selection.

Computational pathomics has emerged as a powerful approach for quantifying the tumor immune microenvironment through automated analysis of whole-slide histopathology images [9]. Deep learning

algorithms can accurately evaluate tumor-infiltrating lymphocytes (TILs), $CD8^+$ cytotoxic T-cell density, stromal composition, tertiary lymphoid structures, immune spatial organization, and tumor architecture. These quantitative immune biomarkers have demonstrated strong associations with clinical response to immune checkpoint inhibitors. When integrated with molecular biomarkers such as programmed death-ligand 1 (PD-L1) expression, tumor mutational burden (TMB), microsatellite instability (MSI), and genomic alterations, multimodal AI models significantly improve prediction of immunotherapy responsiveness compared with single-modality approaches [26].

In melanoma, AI-derived digital biomarkers characterizing immune infiltration patterns and tumor microenvironment architecture have demonstrated promising predictive performance for immune checkpoint inhibitor therapy [9]. Deep learning models identify imaging and histopathological features associated with favorable immunotherapeutic outcomes while simultaneously recognizing characteristics linked to primary or acquired resistance, thereby supporting personalized patient selection and therapeutic optimization.

Similarly, in non-small-cell lung cancer (NSCLC), AI models integrating radiomic biomarkers, genomic tumor mutational burden, and immune-related molecular features provide accurate prediction of immunotherapy benefit [27]. Studies have shown that tumors exhibiting both high radiomic heterogeneity and elevated tumor mutational burden respond more favorably to immune checkpoint blockade than tumors with comparable genomic alterations but lower imaging heterogeneity. These findings highlight the critical role of the tumor microenvironment in modulating genomic determinants of therapeutic response and emphasize the value of multimodal AI for precision immuno-oncology.

Overall, AI-integrated immuno-oncology enables comprehensive characterization of tumor–immune interactions, facilitating individualized immunotherapy selection, early identification of resistance mechanisms, and improved clinical outcomes.

17. Preventive Oncology and Population Screening

Preventive oncology seeks to reduce cancer incidence and mortality through risk assessment, early detection, and timely intervention before the development of symptomatic disease [25]. AI-integrated cancer ecosystems support this objective by combining genetic, molecular, imaging, clinical, and lifestyle information to generate individualized cancer risk profiles that guide personalized prevention and screening strategies.

AI-based risk prediction models integrate germline genetic variants, polygenic risk scores, imaging biomarkers, environmental exposures, lifestyle characteristics, and clinical history to estimate an individual's future cancer risk with greater accuracy than conventional statistical models [25]. In breast cancer, for example, multimodal deep learning models incorporating BRCA1/BRCA2 mutations, polygenic risk scores, mammographic breast density, prior imaging findings, hormonal exposure, and demographic variables demonstrate significantly improved discrimination of future cancer risk compared with traditional clinical nomograms [3].

These individualized risk estimates facilitate risk-adapted population screening, in which screening intensity is tailored according to each patient's predicted risk profile. High-risk individuals may undergo earlier and more frequent surveillance, whereas average-risk individuals continue with standard screening intervals, and low-risk populations may safely undergo less intensive screening [25]. Such personalized approaches improve early cancer detection while reducing false-positive findings, unnecessary diagnostic procedures, overdiagnosis, psychological distress, and healthcare costs. Furthermore, AI-driven screening systems distinguish biologically aggressive cancers requiring immediate intervention from indolent lesions suitable for active surveillance, thereby improving the efficiency and effectiveness of population screening programs [27].

Colorectal cancer screening represents a particularly successful application of AI-assisted prevention. Deep learning algorithms integrated into colonoscopy systems detect adenomatous polyps with sensitivity and specificity comparable to—or exceeding—those of experienced endoscopists, especially for diminutive, flat, and sessile lesions that are frequently overlooked during routine examinations [9]. AI-assisted analysis of polypectomy specimens further predicts recurrence risk and supports individualized surveillance scheduling [25]. Additionally, integration of stool-based multi-omics biomarkers, imaging findings, and genetic susceptibility scores enables non-invasive pre-colonoscopy risk stratification, thereby reducing unnecessary invasive procedures among individuals at low risk while prioritizing high-risk populations for comprehensive diagnostic evaluation [3].

Collectively, AI-integrated preventive oncology is shifting healthcare from reactive disease management toward proactive, individualized cancer prevention through personalized risk assessment, adaptive screening, and early intervention.

18. Explainable AI and Clinical Decision Support

Successful clinical implementation of AI-integrated cancer ecosystems depends not only on predictive accuracy but also on transparency, interpretability, and clinician trust. Explainable artificial intelligence (XAI) provides methods for understanding the reasoning underlying AI-generated predictions, thereby facilitating clinical validation, regulatory approval, and responsible integration into routine oncology practice [27].

Modern deep learning models frequently function as complex "black boxes," limiting clinicians' ability to understand why specific predictions are generated. Explainable AI addresses this challenge by identifying the imaging regions, pathological structures, genomic alterations, or clinical variables that contribute most strongly to individual predictions [9]. Attention mechanisms incorporated within Vision Transformers and multimodal fusion architectures naturally provide interpretable visualizations of model decision-making by highlighting diagnostically important regions within medical images or emphasizing influential molecular features.

Radiomics-based explainable AI identifies intratumoral regions associated with treatment resistance, metastatic potential, and poor prognosis, thereby enabling clinicians to recognize biologically aggressive tumor

compartments that may require intensified therapy [25]. Similarly, computational pathology employs visualization techniques such as attention heatmaps, Gradient-weighted Class Activation Mapping (Grad-CAM), and integrated gradients to highlight diagnostically relevant tissue regions on whole-slide images, allowing pathologists to verify AI-derived predictions against established histopathological criteria and facilitating continuous refinement of computational models [3].

Integration of explainable AI into clinical decision-support systems enhances physician confidence by combining individualized AI predictions with evidence-based treatment guidelines and established clinical pathways [27]. These systems simultaneously analyze genomic alterations, radiological findings, pathological characteristics, and patient-specific clinical variables to generate transparent therapeutic recommendations at the point of care. By reducing cognitive complexity while maintaining clinical interpretability, explainable AI enables oncologists to make more informed, personalized, and evidence-based treatment decisions for increasingly complex cancer patients [9].

19. Federated Learning and Privacy-Preserving Oncology AI

Development of robust AI models for oncology requires access to large, diverse, and representative datasets encompassing medical imaging, genomic sequencing, pathology, and longitudinal clinical outcomes. However, privacy regulations, institutional governance policies, and legal restrictions frequently prevent centralized sharing of sensitive patient information, thereby limiting multicenter collaboration and reducing model generalizability [25].

Federated learning has emerged as a promising solution by enabling collaborative AI model development without transferring patient-level data outside participating institutions [3]. Instead of centralizing clinical datasets, participating healthcare organizations train AI models locally using their own data and share only model parameters or gradient updates with a central coordinating server. These updates are aggregated to improve the global model while ensuring that sensitive patient information remains securely within each institution [27]. Additional privacy-preserving techniques, including differential privacy and secure aggregation, further protect individual patient confidentiality by introducing mathematically controlled noise into locally generated model updates without substantially compromising predictive performance [9].

Federated learning has already demonstrated success in multicenter cancer prediction, radiomics, and computational pathology studies by enabling collaborative model training across geographically diverse healthcare systems. These distributed learning frameworks improve demographic representation, genetic diversity, and clinical generalizability compared with models developed using single-institution datasets, thereby supporting more equitable AI implementation across different patient populations [25].

Complementary blockchain-based data governance frameworks further enhance security by providing transparent, immutable audit trails for data access, model updates, and AI deployment [3]. These technologies improve regulatory compliance, institutional accountability, and trust among collaborating healthcare organizations while ensuring secure management of sensitive biomedical information.

Together, federated learning and privacy-preserving computational frameworks provide the technological foundation for large-scale, multicenter AI development in oncology, enabling highly generalizable precision cancer models while maintaining patient confidentiality, institutional autonomy, and compliance with evolving regulatory standards [27].

20. Ethical, Regulatory, and Data Governance Challenges

The implementation of AI-integrated cancer ecosystems presents important ethical, regulatory, and data governance challenges that must be addressed to ensure safe, equitable, and trustworthy clinical adoption [9]. Among these, **algorithmic bias** remains one of the most significant concerns. AI models trained on datasets that inadequately represent diverse demographic groups, genetic backgrounds, socioeconomic conditions, or healthcare environments may produce unequal predictive performance across patient populations, thereby perpetuating existing healthcare disparities [25]. Numerous retrospective studies have demonstrated reduced diagnostic accuracy and prognostic performance among underrepresented racial and ethnic groups, highlighting the influence of historical biases embedded within healthcare datasets [3].

Mitigating algorithmic bias requires a comprehensive strategy encompassing the development of diverse and representative training datasets, implementation of fairness-aware machine learning techniques, routine bias detection during model development, and rigorous external validation across geographically and demographically diverse populations [27]. Continuous post-deployment monitoring is equally important to ensure sustained model performance as patient populations and clinical practices evolve. Furthermore, equitable access to AI-enabled oncology services requires addressing disparities in healthcare infrastructure, digital resources, and computational capacity so that advances in artificial intelligence benefit resource-limited institutions and underserved communities rather than widening existing inequities [9].

Regulatory oversight of AI-enabled medical technologies continues to evolve rapidly. Agencies such as the **U.S. Food and Drug Administration (FDA)** are developing regulatory frameworks specifically designed for artificial intelligence and machine learning–based medical devices, emphasizing clinical validation, predefined performance specifications, transparency, cybersecurity, and continuous post-market surveillance [25]. However, regulatory requirements remain heterogeneous across international jurisdictions, creating challenges for multinational validation, commercialization, and implementation of AI-driven oncology systems [3]. Greater international harmonization of regulatory standards will be essential to facilitate safe global deployment while maintaining high standards of patient safety and clinical effectiveness [27].

Robust data governance frameworks are equally critical for responsible AI development. Effective governance must balance the need for innovation with patient

privacy, institutional autonomy, transparency, and equitable access to healthcare technologies [9]. Clearly defined policies governing data ownership, informed consent, secondary data use, intellectual property rights, benefit sharing, and cross-institutional collaboration are fundamental to sustainable AI ecosystem development [25]. Moreover, meaningful engagement of patients, clinicians, researchers, policymakers, and healthcare organizations in governance processes ensures that AI systems are developed in accordance with societal values, ethical principles, and public trust rather than solely technical performance metrics [3].

21. Clinical Translation and Future Perspectives

Despite remarkable technological advances, successful translation of AI-integrated cancer ecosystems from research environments into routine clinical practice requires overcoming important technological, organizational, economic, and educational challenges [27]. Although numerous pilot studies have demonstrated the feasibility and clinical value of multimodal AI systems, widespread implementation remains constrained by workflow integration difficulties, regulatory uncertainty, reimbursement limitations, interoperability challenges, and varying levels of clinician acceptance [9]. Sustainable clinical adoption will require close collaboration among oncologists, radiologists, pathologists, bioinformaticians, engineers, policymakers, healthcare administrators, and patients to ensure that AI technologies address genuine clinical needs while integrating seamlessly into existing healthcare infrastructures [25].

Future developments are expected to be driven increasingly by **foundation models**, including large vision models and large language models trained on diverse multimodal biomedical datasets [3]. These highly generalizable models will enable transfer learning across multiple cancer types, imaging modalities, molecular datasets, and healthcare environments while substantially reducing the amount of task-specific annotated data required for model development [27]. In parallel, continued advances in self-supervised learning will enable AI systems to extract meaningful biological representations from large volumes of unlabeled clinical data, thereby accelerating development of specialized applications for rare cancers and resource-limited healthcare settings [9].

Emerging technologies are also expected to facilitate continuous, real-time cancer monitoring through integration of wearable biosensors, liquid biopsy platforms, electronic health records, and digital health technologies [25]. Continuous acquisition of multimodal digital biomarkers combined with adaptive AI algorithms will support dynamic assessment of disease progression, treatment response, toxicity, and survivorship, enabling individualized therapeutic adjustments throughout the entire continuum of cancer care [3]. Furthermore, incorporation of social determinants of health, patient-reported outcomes, behavioral data, and genomic information into multimodal AI frameworks will promote more holistic, patient-centered, and equity-focused precision oncology systems capable of addressing both biological and social determinants of cancer outcomes [27].

Overall, the future of AI-integrated cancer ecosystems lies in the development of continuously learning healthcare platforms that combine multimodal biomedical intelligence with ethical governance, robust clinical validation, and equitable implementation to deliver personalized cancer care at a global scale.

22. Conclusion

AI-integrated cancer ecosystems represent a transformative paradigm in modern oncology by combining multimodal digital biomarkers, advanced computational intelligence, and clinical expertise into unified precision medicine platforms. The integration of radiomics, computational pathology, genomics, multi-omics, liquid biopsy, and longitudinal clinical data through deep learning, transformer architectures, and foundation models enables comprehensive characterization of tumor biology across molecular, cellular, tissue, and clinical levels [9]. These integrated approaches provide more accurate diagnosis, individualized prognostic assessment, optimized therapeutic selection, and continuous disease monitoring than traditional single-modality strategies.

The clinical applications of AI-integrated cancer ecosystems extend across the entire cancer care continuum, including early detection, individualized risk prediction, tumor classification, prognostic modeling, precision therapeutics, immuno-oncology, and preventive cancer medicine. Multimodal AI fusion consistently demonstrates superior predictive performance by integrating complementary biological information from imaging, pathology, molecular profiling, and clinical data, while explainable AI methodologies enhance transparency and strengthen clinician confidence in AI-assisted decision-making [25].

Despite these advances, several challenges continue to limit widespread clinical implementation. Ensuring patient privacy, mitigating algorithmic bias, establishing internationally harmonized regulatory frameworks, improving interoperability, expanding equitable access, and strengthening workforce education remain essential prerequisites for responsible and sustainable AI adoption [3]. Privacy-preserving technologies such as federated learning provide promising solutions for collaborative multicenter AI development while maintaining patient confidentiality and institutional autonomy, thereby facilitating the generation of robust and generalizable oncology models [27].

Looking ahead, the convergence of foundation models, multimodal learning, self-supervised AI, wearable biosensors, liquid biopsy technologies, and continuous digital biomarker monitoring is expected to enable intelligent, adaptive precision oncology ecosystems capable of delivering real-time, individualized cancer care throughout prevention, diagnosis, treatment, and survivorship. Achieving this vision will require sustained multidisciplinary collaboration, rigorous clinical validation, transparent ethical governance, and an unwavering commitment to equity and patient-centered innovation. Collectively, these advances have the potential to transform oncology into a continuously learning, data-driven discipline that improves early detection, personalizes treatment, reduces healthcare

disparities, and ultimately enhances cancer outcomes for patients worldwide.

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