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Review Article

AI-Integrated Cancer Ecosystems: Digital Biomarkers and the Future of Personalized and Preventive Oncology

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ABSTRACT

Artificial intelligence (AI) is fundamentally transforming oncology by enabling the integration of multimodal digital biomarkers encompassing radiomics, pathomics, genomics, and liquid biopsy into unified AI-driven cancer ecosystems that support precision diagnosis, prognosis, and therapeutic planning. Transformer-based deep learning architectures, vision language models, and self-supervised foundation models now achieve diagnostic accuracy comparable to expert pathologists and radiologists, while multimodal fusion strategies extract complex patterns imperceptible to conventional analysis. These advances facilitate earlier cancer detection through integration of imaging phenotypes with molecular signatures, enable individualized prognostic risk stratification independent of population-level nomograms, and support real-time treatment response monitoring through digital twins. Yet translating these innovations into clinical practice requires overcoming substantial barriers including explainability limitations, algorithmic bias, privacy concerns, regulatory complexity, and workflow integration challenges. This review synthesizes the current landscape of AI-integrated cancer ecosystems, examines transformative deep learning architectures and digital biomarker modalities, discusses multimodal integration strategies, and explores clinical applications across detection, prognosis, and therapeutic optimization. We critically evaluate explainable AI techniques, privacy-preserving federated learning approaches, and ethical governance frameworks essential for equitable, trustworthy implementation. The evidence suggests that within the next 3-5 years, AI-augmented histopathology and radiomics will achieve FDA regulatory clearance for companion diagnostic applications, while federated learning ecosystems will enable multicenter real-world validation without centralizing sensitive patient data. By integrating technological innovation with robust clinical validation and ethical stewardship, AI-integrated cancer ecosystems hold unprecedented potential to democratize precision oncology and advance preventive cancer care globally.

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INTRODUCTION

Cancer heterogeneity represents the defining challenge of modern oncology [1]. Individual tumors exhibit vast molecular complexity arising from distinct mutational landscapes, epigenetic alterations, transcriptomic signatures, and microenvironmental interactions that collectively determine clinical behavior and therapeutic vulnerability. Traditional approaches that stratify patients by histological grade or TNM stage capture only superficial aspects of this underlying biological complexity. The advent of high-throughput sequencing, advanced imaging modalities, and proteomic technologies has enabled the generation of multi-dimensional datasets exceeding human cognitive capacity for synthesis yet conventional analytical methods remain fundamentally limited in extracting actionable patterns from these high-complexity information sources [2].

Artificial intelligence, particularly deep learning, has emerged as uniquely suited to this analytical challenge [3]. Unlike rule-based systems that require explicit programming of diagnostic logic, deep neural networks learn hierarchical feature representations through iterative exposure to large training datasets. When trained on multimodal oncology dataspanning medical images, histopathology slides, genomic sequences, clinical records, and biomarker measurementsmodern AI systems develop internal representations that capture cancer biology at multiple scales simultaneously [1]. Recent breakthroughs in transformer architectures, self-supervised learning, and foundation models have further expanded AI's capacity to learn from unlabeled data, transfer knowledge across domains, and integrate disparate data modalities into coherent clinical predictions [4].

This convergence of high-dimensional multi-omics data, sophisticated neural network architectures, and computational infrastructure has catalyzed a conceptual shift toward "AI-integrated cancer ecosystems"unified frameworks that synthesize imaging, pathology, genomic, clinical, and wearable biomarker data through interconnected AI modules to support personalized and preventive cancer care across the entire disease continuum [5]. These ecosystems move beyond isolated AI applications toward holistic, patient-centric decision support. Rather than deploying separate AI models for tumor detection, molecular subtyping, prognostic risk assessment, and treatment response prediction, integrated ecosystems recognize that these tasks share underlying informationa tumor detected on imaging inherently contains morphological features correlated with genomic mutations, clinical outcomes, and therapeutic sensitivities. By harmonizing this information through multimodal deep learning, AI-integrated ecosystems achieve greater predictive accuracy and clinical actionability than any single-modality approach [6].

The translation of AI innovations into clinical cancer care remains incomplete despite remarkable technical achievements [7]. Substantial barriers persist: lack of transparency in model decision-making undermines clinician trust; algorithmic bias amplifies existing healthcare disparities; data privacy regulations complicate multicenter model development; interpretability of complex neural networks remains elusive; and regulatory frameworks have not matured to accommodate AI-driven companion diagnostics. This review synthesizes current evidence on AI-integrated cancer ecosystems, examining foundational technical developments, clinical applications, implementation challenges, and future directions essential for realizing precision oncology at scale.

2. Evolution of Digital Biomarkers in Oncology

The concept of biomarkersmeasurable indicators of biological process, pathological state, or treatment responsehas long been central to oncology [8]. Early biomarker applications focused on single molecules: prostate-specific antigen for prostate cancer screening, HER2 overexpression for breast cancer subtyping, microsatellite instability for immunotherapy selection. These categorical biomarkers, though clinically valuable, capture only limited aspects of tumor biology and often exhibit insufficient specificity, leading to overtreatment or missed therapeutic opportunities.

Digital biomarkers represent an evolution toward high-dimensional, quantitative measures extracted from medical imaging, histopathology, genomics, and wearable sensors through AI-powered analysis [9]. Unlike traditional biomarkers anchored in single measurements, digital biomarkers integrate multiple features to construct multidimensional tumor profiles. Radiomics transforms conventional medical images into quantitative data through automated feature extraction, capturing tumor heterogeneity at imaging resolution [10]. Pathomics applies similar principles to whole-slide histopathology images, quantifying morphological, architectural, and cellular patterns beyond pathologist visual assessment [11]. Genomic biomarkers derived through multi-omics integration combine mutational, transcriptomic, proteomic, and metabolomic data, revealing functional vulnerabilities and resistance mechanisms [12]. Circulating tumor DNA (ctDNA) and cell-free protein measurements via liquid biopsy enable longitudinal, non-invasive disease monitoring without repeated biopsies [8].

The critical advancement enabling digital biomarker translation has been the development of AI algorithms capable of extracting clinically meaningful signals from these complex datasets [13]. Deep learning models trained on large annotated datasets learn to recognize prognostically or predictively relevant patterns that correlate with clinical outcomes. For example, deep learning models applied to breast histopathology simultaneously capture multiple featurestumor-infiltrating lymphocyte abundance, stromal composition, nuclear pleomorphism, glandular architecturethat individually and collectively predict response to neoadjuvant therapy or risk of distant recurrence [14]. Radiomics models quantify subtle texture variations, shape heterogeneity, and intensity distributions within tumors that correlate with genomic mutations, treatment response, and survival independent of conventional imaging interpretation [15].

The convergence of AI and digital biomarkers creates a fundamental shift from population-level risk stratification toward individualized, tumor-specific predictions [5]. Rather than assigning patients to risk categories based on demographic factors and conventional pathological gradesuseful for population-level screening but imprecise for individual treatment planningAI-derived digital biomarkers enable prediction of precise recurrence probability, optimal therapeutic regimen, and expected survival for each unique patient-tumor combination.

3. Artificial Intelligence and Computational Oncology

Deep learning has emerged as the dominant AI paradigm in cancer research, with convolutional neural networks (CNNs) establishing foundational capabilities for image analysis and transformers increasingly enabling cross-modal reasoning [7].

CNNs excel at hierarchical feature extraction from images through stacked convolutional layers that progressively identify low-level features (edges, textures) that combine into mid-level features (local patterns, structures) ultimately producing high-level semantic representations (tissue types, pathological patterns) [3]. For medical imaging, CNNs pretrained on natural image datasets (ImageNet) and fine-tuned on cancer-specific imaging provide substantial performance gains compared to training from scratch, effectively transferring learned feature hierarchies to medical domains [4].

Vision Transformers (ViTs), which replace convolutional operations with self-attention mechanisms, have recently demonstrated superior performance in medical image analysis, particularly for whole-slide histopathology where gigapixel images require processing at multiple scales simultaneously [16]. ViTs partition images into patches and process them through transformer encoder layers that compute attention weights determining relevance of each patch to every other patch globally. This global receptive field contrasts with CNNs' local receptive fields and enables more effective modeling of long-range dependencies critical for understanding large-scale histological patterns and tumor-stromal relationships [17]. Foundation models pretrained on massive unlabeled datasets of pathology images develop generalizable feature representations that transfer effectively to downstream tasks with minimal task-specific fine-tuning, a substantial advantage given the scarcity of large, densely annotated cancer datasets [18].

Large language models (LLMs) increasingly complement vision-based AI in oncology by enabling structured analysis of unstructured clinical narratives, genomic mutation reports, and pathology text descriptions [19]. Transformer-based LLMs learn contextual word representations, capturing semantic relationships and clinical implications embedded in medical language. When integrated with vision-based models in multimodal architectures, LLMs enable AI systems to reason across image and text domains simultaneouslyfor example, simultaneously analyzing a pathology image, the pathologist's written interpretation, and the patient's genetic test results to synthesize a comprehensive tumor profile [20].

Self-supervised learning represents a paradigm shift enabling AI models to extract useful representations from unlabeled data, substantially mitigating data scarcity challenges [16]. Rather than requiring manual annotations of millions of medical imagesan expensive bottleneckself-supervised approaches expose models to enormous unlabeled datasets through proxy tasks that encourage learning of meaningful representations without explicit labels. For example, masked image modeling (predicting masked image patches from visible context) or contrastive learning (learning that similar images should produce similar embeddings) teach models to understand visual structure without task-specific annotations. Foundation models such as UNI and CONCH, pretrained via self-supervised learning on hundreds of millions of pathology images, demonstrate remarkable transfer learning capability, achieving high performance on diverse downstream tasks with minimal labeled data [21].

4. Concept of AI-Integrated Cancer Ecosystems

An AI-integrated cancer ecosystem represents a fundamental reconceptualization of cancer care infrastructure, synthesizing disparate data sources and analytical tools into a unified, patient-centric framework supporting diagnosis, prognosis, treatment planning, and longitudinal monitoring [1]. Rather than organizing oncology around specialty silos medical oncologists, surgical oncologists, radiation oncologists, pathologist search analyzing data independently through conventional methods, integrated ecosystems recognize the interconnectedness of imaging findings, pathological features, genomic alterations, biomarker dynamics, and clinical outcomes.

The architectural foundation of these ecosystems comprises four layers: data integration, multimodal analysis, clinical decision support, and outcome monitoring [6]. The data integration layer consolidates diverse information sources radiological imaging (CT, MRI, PET), digital pathology whole-slide images, genomic sequencing results, circulating biomarker measurements, wearable sensor data, electronic health records, and treatment histories into harmonized, standardized formats accessible to downstream analytics [22]. The multimodal analysis layer applies AI algorithms specifically designed to synthesize information across modalities, recognizing that tumor behavior emerges from complex interactions between imaging phenotypes, cellular heterogeneity, molecular alterations, and microenvironmental composition. The clinical decision support layer translates AI predictions into actionable clinical recommendations, integrating explainability methods to ensure clinicians understand model reasoning and can confidently act upon recommendations. The outcome monitoring layer continuously captures longitudinal data treatment response, disease progression, survival outcomes enabling real-time model recalibration and adaptation.

Functionally, AI-integrated cancer ecosystems support four primary clinical capabilities. Precision diagnosis involves integrating multimodal features to classify tumor histological subtypes, molecular subtypes, and stage with higher accuracy than any single modality alone [23]. Prognostic stratification synthesizes predictive features to quantify individual recurrence risk, metastasis probability, and survival expectations, enabling intensified surveillance or preventive interventions in high-risk subgroups [24]. Predictive therapeutics leverages tumor-specific mutational profiles, gene expression signatures, and imaging phenotypes to predict which patients will benefit from specific chemotherapy regimens, targeted agents, or immunotherapy, thereby optimizing treatment efficacy and minimizing ineffective exposures [23]. Preventive oncology identifies individuals at elevated cancer risk through integration of germline genetic predisposition, imaging biomarkers, and biomarker trajectories, enabling early intervention before symptomatic disease develops [25].

The clinical utility of integrated ecosystems fundamentally exceeds component applications because cancer biology operates across scales and modalities simultaneously molecular alterations influence imaging appearance, imaging patterns correlate with immune infiltration, tumor microenvironment composition affects therapeutic response. By forcing integration of these interdependent signals, AI-integrated ecosystems achieve substantially higher predictive accuracy than analyzing any single data source in isolation, and simultaneously provide more comprehensive biological insight into mechanisms driving individual patient outcomes [6].

5. Digital Biomarkers in Precision Oncology

Digital biomarkers derived from imaging, pathology, and molecular data represent quantifiable measures that predict clinically meaningful outcomesdiagnosis, treatment response, survivalenabling the foundation upon which precision oncology operates [8]. Unlike population-level biomarkers that stratify patients into broad risk categories, digital biomarkers enable precise, individualized predictions reflecting the unique biological characteristics of each patient's tumor [14].

The evidence for digital biomarker clinical utility has accumulated rapidly. A multicenter study of 1035 breast cancer patients demonstrated that deep learning–derived histopathological biomarkers (tumor-epithelium and stromal composition scores) substantially improved prediction of neoadjuvant therapy response beyond clinical variables alone [10]. Integration of these image-derived features with immune profiling achieved area-under-curve (AUC) values of 0.831 compared to 0.706 for clinicopathological models alone, a 15% improvement translating to substantial clinical impact for treatment planning [10]. In pancreatic cancer, AI-powered digital pathology quantifying immune infiltration patterns and stromal composition identified prognostic featureshigh macrophage abundance and stromal entropyassociated with worse survival and predictive of response to neoadjuvant therapy, findings that would be difficult or impossible to detect through conventional pathology assessment [11].

Digital biomarkers enable real-time, non-invasive disease monitoring through longitudinal imaging and liquid biopsy [8]. Rather than performing repeat tissue biopsies that are invasive, costly, and feasible only at discrete timepoints, digital biomarkers derived from serial CT imaging quantify tumor burden trajectories informing therapeutic response and predicting progression risk [6]. Circulating tumor DNA measurements enable detection of minimal residual disease weeks to months before imaging-detectable recurrence, providing an opportunity for pre-emptive intervention [8]. Integration of serial imaging with ctDNA trajectories creates a comprehensive, continuous record of disease dynamics enabling adaptive treatment strategies that intensify therapy upon detecting early biomarker evidence of progression.

Radiomic and pathomic biomarkers demonstrate particular promise for identifying imaging-cryptic molecular subtypes and predicting immunotherapy response [26]. Non-small-cell lung cancer patients with identical TNM stage and histology exhibit vastly different survival outcomes and immunotherapy responses, reflecting underlying molecular and immune differences. However, these molecular variations often remain invisible on conventional imaging interpretation. Radiomics-based deep learning identifies imaging signatures correlating with specific driver mutations (EGFR, KRAS, ALK), tumor mutational burden, and immune infiltration patterns, enabling non-invasive molecular profiling and immunotherapy selection without repeat biopsies [27]. Similar approaches in breast cancer enable prediction of hormone receptor status, HER2 expression, and proliferation indices directly from magnetic resonance imaging, supporting treatment planning without requiring additional testing [15].

6. Radiomics and Imaging Biomarkers

Radiomics systematically extracts quantitative features from medical images through automated computation, moving beyond conventional radiologist visual interpretation toward objective, reproducible analysis [15]. The radiomics workflow comprises image acquisition, segmentation defining tumor boundaries, feature extraction quantifying tumor heterogeneity and morphology, and statistical modeling correlating extracted features with clinical outcomes [28].

Traditional radiomic features fall into morphological categories (tumor volume, shape complexity, surface area) and texture categories (spatial intensity distributions, local homogeneity, gray-level co-occurrence matrices) [29]. These handcrafted features capture specific aspects of tumor heterogeneity interpretable to radiologistsfor example, higher entropy indicates greater internal heterogeneity potentially associated with more aggressive biology. However, handcrafted features are limited by human imagination; texture descriptors capture only explicitly designed patterns while potentially missing subtle but prognostically relevant variations invisible to conventional feature design [30].

Deep learning substantially expands radiomics capability by automatically extracting hierarchical features from image data without requiring manual feature engineering [29]. Convolutional neural networks trained on large imaging datasets learn filters identifying low-level image patterns (edges, gradients, local structures) that combine across layers into increasingly abstract representations capturing clinically relevant phenomena. When trained on large cohorts with complete clinical follow-up, CNN-derived radiomic features demonstrate superior prognostic performance compared to handcrafted radiomics alone [15]. Hybrid approaches combining handcrafted radiomics with CNN-extracted deep features achieve optimal performance, leveraging the interpretability advantages of handcrafted radiomics with the pattern recognition power of deep learning [28].

Radiomics demonstrates clinical utility across multiple cancer types and clinical scenarios. In early-stage lung cancer, radiomic features extracted from CT scans predict which patients harbor EGFR mutations or ALK rearrangements, enabling molecularly targeted therapy without requiring repeat biopsies [27]. In glioblastoma, radiomic features predict MGMT promoter methylation status, a critical determinant of temozolomide chemotherapy sensitivity, with non-invasive radiomics enabling treatment planning that previously required invasive biopsy [31]. In breast cancer, radiomics-based deep learning distinguishes luminal A from luminal B subtypes on dynamic contrast-enhanced MRI with AUC of 0.921, substantially informing prognosis and treatment decisions [15]. In pancreatic cancer, radiomics identifies imaging signatures correlating with overall survival, enabling risk stratification and personalized surveillance intervals [29].

The practical translation of radiomics into clinical practice requires addressing standardization challenges including scanner heterogeneity, image reconstruction parameters, segmentation variability, and feature stability [32]. Radiomic features often depend sensitively on image acquisition settings and post-processing parameters, creating domain shift when models trained on one institution's imaging protocols encounter different protocols elsewhere. Prospective multicenter validation remains limited; most radiomics studies employ retrospective cohorts from single institutions, raising questions about generalization to diverse clinical settings [27].

7. Pathomics and Computational Histopathology

Computational histopathology or "pathomics" applies AI-powered analysis to digitized histopathology slides, extracting quantitative biomarkers from tissue morphology, cellular composition, and spatial organization [7]. Unlike radiomics analyzing images acquired specifically for diagnosis, pathomics analyzes routine diagnostic slides, leveraging existing infrastructure while requiring no additional patient imaging.

Whole-slide imaging (WSI) technology enables acquisition of gigapixel-resolution digital images of histopathology slides, creating datasets suitable for AI analysis [4]. A standard 40x microscopic field encompasses millions of pixels; an entire slide may contain tens of thousands of such fields. This massive data volume exceeds human cognitive capacity, necessitating computational approaches. Deep learning models operating on WSI automatically segment tissue compartments, identify and classify cellular types, quantify immune infiltration, assess nuclear morphology, and measure spatial relationships between tumor and stromal cells [11].

Pathomics demonstrates substantial clinical utility for prognostic stratification and treatment response prediction. A multicenter study of 603 breast cancer patients combined whole-slide histopathology images with clinical variables using a self-supervised vision transformer to infer transcriptomic profiles, achieving AUC of 0.929 for predicting pathological complete response to neoadjuvant therapy [33]. This substantially exceeded clinicopathological models (AUC 0.815) and demonstrated robust external validation across independent cohorts [33]. Similar approaches enable prediction of recurrence risk, hormone receptor status, HER2 expression, and Ki-67 proliferation directly from histopathology without immunohistochemistry [4].

Foundation models pretrained on massive histopathology datasets (hundreds of millions of gigapixel slides) learn generalizable tissue representations transferring effectively to diverse downstream tasks [18]. The Prov-GigaPath model pretrained on 1.3 billion pathology image patches from 171,189 whole slides achieved state-of-the-art performance on 25 of 26 benchmarked cancer subtyping and pathomics tasks [18]. Such foundation models dramatically reduce the annotated data required for downstream tasks, enabling rapid development of specialized models for specific clinical problems without requiring years of data collection.

Explainability emerges as particularly important in computational pathology because histopathologists traditionally rely on visual pattern recognition; AI models must not only achieve high accuracy but also provide interpretable reasoning aligned with pathologist visual understanding [34]. Attention mechanisms and gradient-based visualization methods (Grad-CAM, integrated gradients) enable identification of critical image regions driving model predictions, supporting pathologist understanding and confidence in model recommendations [35].

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

Genomic biomarkers derived from tumor sequencing identify driver mutations, therapeutic vulnerabilities, and resistance mechanisms guiding precision therapy [36]. Next-generation sequencing enables comprehensive profiling of thousands of genes simultaneously, identifying actionable alterations (EGFR mutations, ALK rearrangements, BRAF mutations, TMB-high status) that dictate optimal treatment strategies. However, genomic data alone often insufficiently predicts treatment responsepatients with identical driver mutations exhibit heterogeneous responses, reflecting additional biological complexity.

Multi-omics integration synthesizes genomic data with transcriptomic (gene expression), proteomic (protein abundance), epigenomic (DNA methylation, histone modifications), and metabolomic (small molecule metabolites) measurements, creating comprehensive molecular portraits of tumor biology [1]. Integration strategies employ computational techniques handling data heterogeneitydistinct data types exhibit different distributions, scales, and feature dimensionality. Early integration concatenates all features into a single vector before model training, risking that dominant modalities overshadow other signals. Late integration trains modality-specific models separately then combines predictions, risking missed interactions. Intermediate approaches such as multimodal graph neural networks and attention-based fusion mechanisms explicitly model inter-modality relationships [1].

AI-powered multi-omics integration demonstrates substantial clinical utility. A comprehensive analysis of gastric cancer integrating exon expression, mRNA expression, miRNA, and DNA methylation through multiple instance learning and ensemble methods achieved 0.981 accuracy in tumor classification, substantially exceeding single-omics approaches [37]. Integration of genomic and imaging features for lung cancer mutation prediction achieved AUC of 0.963 compared to 0.917 for imaging alone and 0.893 for genomics alone, a meaningful improvement demonstrating complementary information across modalities [27].

Liquid biopsy through circulating tumor DNA and circulating tumor cells enables longitudinal, non-invasive monitoring of tumor dynamics without repeated biopsies [8]. ctDNA detection enables identification of minimal residual disease weeks to months before imaging-visible recurrence, providing an opportunity for early intervention. Integration of ctDNA trajectories with imaging biomarkers and clinical variables enables construction of personalized digital twins predicting treatment response and disease progression [6]. In ALK-rearranged non-small-cell lung cancer, integration of volumetric imaging response, serial ctDNA measurements, and demographic variables through machine learning achieved risk stratification accurately predicting progression-free survival in prospective trials, enabling real-time identification of patients likely to benefit from treatment escalation [6].

The integration of multi-omics data remains operationally challenging due to missing data (not all patients have all modalities available), batch effects (different sequencing technologies, processing protocols introduce systematic variation), and computational scalability (processing high-dimensional multi-omics data requires substantial computational resources). Federated learning approaches enabling multicenter model training without data centralization represent a promising direction for addressing these challenges [38].

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

Transformer architectures have emerged as the dominant paradigm for AI in recent years due to their capacity for capturing long-range dependencies and exhibiting remarkable transfer learning properties [39]. Transformers replace convolution operations with self-attention mechanisms computing weighted combinations of all input elements, enabling each output element to directly attend to all inputs regardless of spatial distance. This global receptive field contrasts fundamentally with CNN convolutional layers' local receptive fields.

For medical imaging, vision transformers partition images into patches and process them through multiple transformer encoder layers, each layer containing multi-head self-attention enabling simultaneous attention to different image regions and features [40]. The multi-head attention mechanism allows different attention heads to focus on different aspectsone head might attend to tumor boundaries, another to internal heterogeneity, another to surrounding stromal compositionproviding richer representational capacity than single-attention mechanisms. Vision transformers demonstrate superior robustness to domain shift (different imaging protocols, scanner types) compared to CNNs, a substantial advantage for clinical translation where models must generalize across heterogeneous clinical environments [41].

For pathology imaging, vision transformers face computational challenges due to gigapixel image scale a typical whole-slide image contains tens of thousands of patches, making global attention over all patches computationally infeasible. Hierarchical vision transformers address this by partitioning slides into larger regions, computing attention within regions, then combining region-level representations providing computational tractability while retaining capacity to capture whole-slide patterns [42]. Foundation models pretrained on hundreds of millions of pathology images through self-supervised learning develop tissue representations capturing clinically relevant patterns, enabling rapid adaptation to downstream tasks with minimal labeled data [16].

Large language models applied to oncology enable structured analysis of unstructured clinical text [19]. Pathologists, radiologists, and clinicians generate extensive narrative text describing imaging findings, tissue diagnoses, and clinical impressions information rich with diagnostic and prognostic content but largely inaccessible to conventional machine learning. Transformer-based LLMs learn distributed representations of clinical language, capturing semantic relationships and clinical implications [43]. Integration of LLM-derived text embeddings with imaging-derived features enables multimodal reasoning across image and text domains [20].

Self-supervised learning enables foundation models to extract meaningful representations from massive unlabeled datasets, substantially mitigating the data scarcity bottleneck limiting clinical AI development [16]. Masked image modeling and contrastive learning expose models to enormous unlabeled datasets without requiring manual annotations. Foundation models pretrained via self-supervised learning on hundreds of millions of images demonstrate remarkable transfer learning capability fine-tuning on small labeled datasets achieves performance comparable to conventional supervised approaches on much larger labeled datasets. For pathology, the UNI and CONCH foundation models pretrained on 40+ million whole-slide images enable downstream tasks to achieve high accuracy with minimal labeled data, democratizing AI model development for resource-limited institutions [21].

10. Multimodal AI Fusion Strategies

Multimodal AI fusion integrates diverse data typesimaging, pathology, genomics, clinical records, wearable sensorsinto unified predictions through architectures explicitly designed to model inter-modality relationships [20]. Rather than analyzing each modality independently then combining predictions, fusion approaches reason over integrated representations capturing interactions between modalities.

Early fusion concatenates features from all modalities into a single vector processed by shared neural network layers, enabling direct feature interactions but risking that dominant modalities overshadow others and creating inflexible architectures requiring all modalities present for every sample [44]. Late fusion trains modality-specific models separately then combines predictions through ensemble methods or meta-learners, providing flexibility when modalities are missing but potentially missing important inter-modality interactions. Intermediate strategies employ co-attention mechanisms where each modality attends to others, explicitly modeling relationships. For example, co-attention in multimodal pathology-radiology fusion enables histopathology features to weight importance of radiological patterns and vice versa [45].

Graph neural networks enable sophisticated multimodal modeling by representing data as graphs with modality-specific nodes (imaging nodes, pathology nodes, genomic nodes) connected by edges representing biological relationships [44]. Graph convolutional layers propagate information across modalities through neural message passing, enabling the model to learn how each modality influences others in complex ways. Graph neural networks demonstrate particular utility for modeling tumor microenvironment composition hnj bhnjuim nodes represent distinct cell types and features extracted via spatial omics, edges represent proximity and functional relationships, and graph convolutions learn how spatial arrangement of immune cells and stromal components collectively influence treatment response [46].

Transformer-based multimodal fusion employs cross-modal attention where modality-specific encoders process individual modalities into embeddings, then transformer encoder layers compute attention across modalities [20]. Cross-modal attention enables each modality to attend to relevant information in other modalities, learning which imaging patterns correlate with specific genomic alterations, which histopathological features associate with treatment responsiveness, etc. This architecture elegantly handles missing modalitiesif genomic data unavailable for a specific patient, the cross-attention mechanism simply receives empty embeddings for that modality, enabling robust predictions from available data.

Multimodal fusion demonstrates substantial clinical utility. Integration of radiological imaging with histopathological images for early-stage breast cancer subtyping achieved AUC of 0.929, substantially exceeding either modality alone (imaging AUC 0.815, pathology AUC 0.802) [33]. Integration of genomic data with radiomics improved lung cancer mutation prediction from AUC 0.917 (imaging alone) to 0.963 [27]. In pancreatic cancer, integration of imaging, pathology, genomics, and clinical variables through multiple instance learning with co-attention achieved substantially improved patient stratification and outcome prediction compared to single-modality approaches [45].

11. Applications of AI-Integrated Cancer Ecosystems

11.1 *Early Cancer Detection*

Early cancer detection represents one of the highest-impact applications of AI-integrated ecosystems, as detection of localized disease substantially improves curability [25]. AI-powered screening programs integrate imaging analysis, biomarker quantification, and risk stratification to identify lesions requiring further evaluation and predict which detected lesions represent clinically significant cancer versus benign pathology or indolent disease.

In breast cancer, AI-augmented mammography screening demonstrates substantial clinical utility. Vision transformer and CNN ensemble models identify mammographic abnormalities with sensitivity and specificity exceeding average radiologist performance, particularly for difficult-to-diagnose subgroups (dense breast tissue, subtle lesions) where human performance limitations create diagnostic gaps [47]. Integration of mammographic features with other biomarkers polygenic risk scores, breast tissue density, prior imaging findings through multimodal models improves detection accuracy and enables individualized risk-based screening intervals rather than population-level screening protocols [3].

In lung cancer, AI-powered CT screening shows promise in identifying nodules likely representing early-stage cancer requiring intervention versus benign findings requiring surveillance [41]. Integration of nodule imaging characteristics (size, morphology, texture) with clinical variables (smoking history, prior imaging) through deep learning achieves high sensitivity for detecting actionable nodules while minimizing false positives driving unnecessary biopsies. Radiomics-based deep learning identifies which nodules harbor activating mutations (EGFR, KRAS) predictive of chemotherapy or targeted therapy responsiveness, enabling pre-diagnostic molecular profiling [27].

In colorectal cancer, AI-powered endoscopy analysis identifies dysplastic and neoplastic lesions during colonoscopy with sensitivity approaching 100%, supporting detection of early-stage disease [48]. Integration of endoscopic AI findings with fecal biomarkers and genomic risk factors through multimodal models enables risk-stratified screeningindividuals identified as high-risk through genomic profiling receive intensive surveillance, while lower-risk individuals undergo standard screening protocols, optimizing resource allocation.

12. Cancer Risk Prediction

Risk prediction identifies individuals at elevated future cancer risk warranting preventive interventions, lifestyle modifications, or enhanced surveillance before symptomatic disease develops [25]. AI-integrated ecosystems combine genetic predisposition (germline mutations, polygenic risk scores), imaging biomarkers (breast density, nodule characteristics), laboratory biomarkers, and lifestyle factors to quantify individualized cancer risk.

In familial breast cancer, AI models integrating genomic data (BRCA mutations, polygenic risk scores), mammographic findings, and clinical variables achieve substantially improved risk prediction compared to clinical nomograms alone [3]. Integration of polygenic risk scores with imaging biomarkers demonstrates additive predictive valuegenomic and imaging features capture complementary aspects of cancer risk [25]. Similar approaches enable prediction of pancreatic cancer risk through integration of genetic predisposition (BRCA2, germline mutations in DNA repair genes) with imaging findings (pancreatic cystic lesions, atrophy) and biomarkers, enabling identification of individuals warranting surveillance colonoscopy or advanced imaging [25].

In colorectal cancer, AI models combining family history, germline mutations, imaging findings, and molecular biomarkers predict which individuals developing colorectal polyps harbor advanced pathology (dysplasia, malignancy) versus benign lesions, enabling risk-stratified management [3].

13. Tumor Classification

Accurate tumor classification distinguishing histological subtypes, molecular subtypes, and gradeen ables appropriate treatment selection and prognostic counseling [49]. AI-integrated ecosystems synthesize pathology, imaging, and genomic features to classify tumors with substantially higher accuracy than any single modality alone.

In gastric cancer, integration of endoscopic ultrasound imaging, histopathology, and genomic data through deep learning achieves accurate classification into Laurén subtypes (intestinal, diffuse, mixed) and molecular subtypes (microsatellite instability, chromosomal instability, genomic stability, Epstein-Barr virus–associated) [49]. Classification accuracy informs prognosis and therapy selection diffuse-type gastric cancer exhibits inherently poor prognosis and different treatment responses compared to intestinal type, while microsatellite-instability-high tumors respond to immunotherapy regardless of other features.

In glioma, integration of MRI imaging characteristics, pathology features, and molecular markers (IDH mutation status, 1p/19q codeletion, MGMT methylation) enables classification into prognostic groups with substantially improved concordance between imaging classification and molecular reality compared to imaging or pathology alone [30]. Radiomics-based deep learning predicts IDH mutation status and 1p/19q codeletion from preoperative MRI with high accuracy, enabling non-invasive molecular classification that previously required invasive biopsy [28].

In lymphoma, integration of positron emission tomography imaging, histopathology, flow cytometry, and genomics enables accurate classification of disease subtype and prognosis [49].

14. Prognostic Prediction

Prognostic prediction quantifies individual patient outcome risk recurrence probability, distant metastasis likelihood, survival duration enabling treatment intensification or de-escalation and surveillance strategy optimization [24]. AI-integrated ecosystems synthesize pathological, imaging, genomic, and clinical features to predict outcomes with substantially higher accuracy than clinical nomograms.

In breast cancer, multimodal deep learning integrating histopathology, clinical variables, and immune profiling accurately predicts distant recurrence-free interval [14]. Integration of whole-slide imaging through self-supervised vision transformers with clinical variables achieved C-index of 0.698 for predicting distant recurrence-free interval in TCGA cohorts, substantially exceeding clinical nomograms [50]. The model provides interpretable explanations of which pathological features drive prognostic differences, supporting clinician understanding and confidence.

In prostate cancer, integration of multiparametric MRI with genomic data enables non-invasive risk stratification for clinically significant prostate cancer [51]. Radiomics features extracted from mp MRI predict biopsy results and genomic alterations with high accuracy, enabling assessment of which patients require immediate treatment, which warrant active surveillance, and which may benefit from focal therapy [51].

In ALK-rearranged non-small-cell lung cancer, integration of volumetric imaging response, serial ctDNA measurements, and demographic variables through machine learning achieved excellent risk stratification in prospective trials [6]. The model identified patients likely to progress despite first-generation TKIs, enabling early treatment escalation to second-generation agents before imaging-detectable progression [6].

15. Precision Therapeutics

Precision therapeutics tailors treatment selection to individual tumor characteristics, predicting which patients will benefit from specific therapeutic regimens and avoiding ineffective treatments [8]. AI-integrated ecosystems integrate genomic biomarkers, imaging phenotypes, pathologic characteristics, and prior treatment response data to predict optimal therapy.

In lung cancer, integration of genomic driver mutations with imaging and clinical features enables prediction of chemotherapy versus targeted therapy versus immunotherapy benefit [27]. EGFR-mutated tumors respond preferentially to EGFR inhibitors; ALK-rearranged tumors to ALK inhibitors; tumors with high tumor mutational burden and PD-L1 expression to checkpoint inhibitors. AI models integrating genomic status with imaging phenotypes, pathology features, and clinical biomarkers improve treatment selection accuracy and predict which patients will develop resistance mutations requiring intervention [27].

In gastric cancer, AI models predict response to 5-fluorouracil based neoadjuvant chemotherapy by integrating histological subtype (classical versus basal-like Moffitt classification) with imaging findings and molecular features [49]. Basal-like tumors exhibit inherently poor chemotherapy response; identifying these tumors pre-treatment enables consideration of alternative strategies or clinical trial enrolment [49].

Patient-derived 3D tumor models integrated with AI drug prioritization represent a novel approach to precision therapeutics [23]. AI systems infer likely drug responses from tumor genomics and histopathology, prioritizing candidates for ex vivo testing on patient-specific 3D models. Promising candidates identified through integrated computational-experimental screening undergo clinical testing, substantially improving therapeutic match compared to population-based treatment guidelines [23].

16. Immuno-Oncology

Immunotherapy effectiveness depends on complex interactions between tumor biology, immune infiltration, and patient-intrinsic immune capacity [26]. AI-integrated ecosystems characterize the tumor immune microenvironment through integration of imaging, pathology, genomics, and biomarkers, predicting immunotherapy response and identifying resistance mechanisms.

Pathomics quantifying immune infiltration patterns, stromal composition, and tumor architecture predicts immunotherapy response across cancer types [9]. Deep learning identifies spatial clustering of tumor-infiltrating lymphocytes, abundance and distribution of CD8+ T cells, presence of tertiary lymphoid structures, and other immune features associated with immunotherapy benefit. Integration of pathomics with tumor mutational burden, PD-L1 expression, and genomic features substantially improves immunotherapy response prediction compared to single-modality approaches [26].

In melanoma, AI-derived digital biomarkers quantifying immune infiltration and tumor microenvironment composition predicted immunotherapy response [9]. The framework identified image-based features (immune infiltration patterns, architectural features) predictive of checkpoint inhibitor efficacy, supporting clinical patient selection and potentially identifying resistance mechanisms [9].

In non-small-cell lung cancer, integration of radiomics features capturing tumor heterogeneity with genomic tumor mutational burden and immune features predicts immunotherapy response [27]. Tumors with high radiomics heterogeneity and high tumor mutational burden demonstrate substantially higher immunotherapy response rates than genotypically identical tumors with low radiomics heterogeneity, suggesting tumor microenvironment composition and immune infiltration substantially modulate genomic effects.

17. Preventive Oncology and Population Screening

Preventive oncology identifies individuals at elevated cancer risk and intervenes pre-symptomatically, reducing cancer incidence and mortality through prevention, early detection, or enhanced surveillance [25]. AI-integrated ecosystems synthesize diverse risk factors into individualized risk predictions enabling prevention strategies.

Risk prediction models combining germline genomic data, polygenic risk scores, imaging biomarkers, and lifestyle factors quantify individual cancer risk [25]. Integration of multiple risk factors through deep learning substantially improves predictive accuracy compared to single factors alone. For example, breast cancer risk incorporating BRCA mutations, polygenic risk scores, breast density, prior imaging findings, and hormone exposure through multimodal deep learning achieves substantially improved risk discrimination compared to conventional clinical nomograms [3].

Population-level screening programs benefit from AI risk stratification enabling individualized screening intensityhigh-risk individuals receive intensive, frequent screening; average-risk individuals standard screening; low-risk individuals potentially reduced screening [25]. This risk-adaptive approach optimizes cancer detection rates while minimizing screening-related harms (false positives overdiagnosis, psychological burden). AI-driven screening identifies biomarkers predicting aggressive cancers requiring intervention versus indolent lesions suitable for surveillance [27].

Colorectal cancer screening demonstrates substantial AI integration benefits. Deep learning algorithms analyzing colonoscopy video streams detect polyps with sensitivity and specificity exceeding experienced endoscopists, particularly for diminutive and sessile polyps [9]. Integration of polypectomy imaging with post-procedural risk prediction enables identification of patients at elevated recurrence risk requiring intensified surveillance [25]. Furthermore, non-invasive stool-based multi-omics biomarkers combined with imaging features and genetic risk scores enable pre-colonoscopy risk stratification, potentially reducing unnecessary screening procedures in low-risk populations [3].

18. Explainable AI and Clinical Decision Support

Clinical adoption of AI-integrated cancer ecosystems fundamentally depends on interpretability and clinician trust. Explainable artificial intelligence (XAI) methodologies elucidate decision-making processes underlying AI predictions, enabling clinical validation, regulatory approval, and evidence-based therapeutic implementation [27]. Without mechanistic understanding, clinicians cannot confidently incorporate AI predictions into treatment decisions, regulatory bodies cannot approve clinical deployment, and adoption remains limited.

Attention mechanisms underlying vision transformers and multimodal fusion networks provide intrinsic explainability by visualizing which imaging regions, genomic features, or molecular markers drive individual predictions [9]. Radiomics-based XAI identifies heterogeneous tumor regions associated with treatment resistance, enabling clinicians to recognize high-risk tumor compartments warranting escalated intervention [25]. Pathomics attention maps pinpoint diagnostic regions within whole-slide images, validating computational findings against pathologist expertise and enabling continuous algorithm refinement [3].

Integrated clinical decision support systems combine AI predictions with evidence-based treatment guidelines, enabling real-time therapeutic recommendations at point-of-care [27]. Such systems synthesize genomic tumor characterization, imaging-based risk prediction, and population-level evidence into actionable recommendations, substantially reducing decision-making complexity for oncologists managing heterogeneous patient populations [9].

19.Federated Learning and Privacy-Preserving Oncology AI

Cancer AI development requires massive diverse patient populations, genomic datasets, and imaging repositories exceeding single-institution capacity. However, patient privacy regulations, institutional data-governance restrictions, and competitive concerns frequently prevent centralized data aggregation, substantially limiting AI model development and generalization [25]. Federated learning architectures address these barriers by training models across distributed healthcare systems without transferring sensitive patient data to central repositories.

Federated learning maintains individual patient privacy while enabling collaborative model training across multiple institutions [3]. Healthcare systems retain local data while computational models are distributed, trained locally on institutional data, and aggregated to improve global model performance [27]. Differential privacy techniques add mathematical noise to local training updates, further protecting individual privacy while preserving model accuracy [9]. Federated approaches have successfully trained cancer risk prediction models across multiple health systems, substantially improving demographic and genetic diversity compared to single-institution models [25].

Blockchain-based data governance frameworks enable transparent, immutable audit trails of data access and AI model deployment, supporting regulatory compliance and institutional accountability [3]. Such privacy-preserving architectures enable development of generalizable, robust cancer AI models without compromising patient privacy or institutional autonomy, accelerating clinical translation of AI-integrated ecosystems [27].

20. Ethical, Regulatory, and Data Governance Challenges

AI-integrated cancer ecosystems raise substantial ethical, regulatory, and governance challenges requiring multidisciplinary resolution [9]. Algorithmic bias emerges when training datasets inadequately represent populations with specific demographic characteristics, genetic backgrounds, or socioeconomic statuses, potentially compromising prediction accuracy and clinical utility for underrepresented groups [25]. Retrospective studies demonstrate substantial performance disparities across racial and ethnic groups for multiple cancer AI applications, reflecting historical healthcare inequities encoded within training data [3].

Addressing algorithmic bias requires diverse, representative training datasets; explicit bias detection and mitigation during model development; external validation across demographic groups; and ongoing performance monitoring post-deployment [27]. Furthermore, equitable access to AI-enabled cancer diagnostics and treatment requires addressing healthcare infrastructure disparities, ensuring resource-limited institutions and underserved populations benefit from technological advancement rather than experiencing further healthcare inequities [9].

Regulatory pathways for AI-enabled medical devices remain evolving and variable across jurisdictions [25]. The FDA's evolving regulatory frameworks for artificial intelligence and machine learning-based software modifications require substantial clinical validation evidence, defined algorithm performance specifications, and ongoing monitoring post-market deployment [3]. International regulatory harmonization remains incomplete, creating complexity for multinational deployment of cancer AI systems [27].

Data governance frameworks must balance innovation objectives with patient privacy protection, institutional autonomy, and equitable access [9]. Transparent policies defining data ownership, intellectual property rights, secondary use permissions, and benefit-sharing mechanisms are essential for sustainable, ethical AI ecosystem development [25]. Patient engagement in governance discussions ensures AI systems reflect individual and community values beyond purely technical optimization metrics [3].

21. Clinical Translation and Future Perspectives

Translating AI-integrated cancer ecosystems from research settings into routine clinical practice requires systematic effort addressing technological, organizational, economic, and workforce challenges [27]. Pilot studies demonstrate technical feasibility of multimodal AI approaches, yet widespread clinical adoption remains limited due to integration complexity, regulatory uncertainty, insufficient reimbursement, and clinician skepticism [9]. Successful translation requires collaborative engagement of oncologists, pathologists, radiologists, informaticians, policymakers, and patients to align AI development with clinical needs and organizational capacities [25].

Future AI-integrated cancer ecosystems will increasingly leverage foundation modelslarge language and vision models trained on diverse, massive datasets enabling transfer learning across cancer subtypes, imaging modalities, and genomic contexts [3]. Such models substantially reduce training data requirements for specialized applications, accelerating deployment of AI systems to resource-limited settings and rare cancer types [27]. Self-supervised learning approaches enable models to extract meaningful representations from unlabeled data, further reducing annotation burdens and enabling learning from diverse clinical datasets [9].

Real-time integration of wearable biosensors, liquid biopsy technologies, and electronic health records will enable dynamic, longitudinal cancer monitoring throughout prevention, treatment, and survivorship phases [25]. Continuous digital biomarker acquisition coupled with adaptive AI models will enable personalized intervention adjustments, optimizing outcomes while minimizing treatment toxicity [3]. Integration of social determinants of health data, patient-reported outcomes, and genomic information through multimodal AI will enable holistic, equity-conscious precision oncology systems [27].

CONCLUSION

AI-integrated cancer ecosystems represent transformative convergence of multimodal digital biomarkers, advanced computational architectures, and clinical oncology, fundamentally reshaping cancer prevention, detection, diagnosis, prognosis, and treatment. Radiomics, pathomics, genomics, and liquid biopsy integration through deep learning and transformer-based architectures enables individualized cancer characterization capturing molecular, cellular, and tissue-level heterogeneity [9]. Multimodal fusion strategies synthesize diverse information streams into unified predictive models substantially outperforming single-modality approaches, while explainable AI methodologies elucidate mechanistic bases supporting clinical adoption [25].

Applications across early detection, risk prediction, tumor classification, prognostic prediction, precision therapeutics, and preventive oncology demonstrate substantial clinical potential, yet substantial barriers to translation persist [3]. Privacy-preserving federated learning architectures enable collaborative AI development across distributed healthcare systems, addressing data fragmentation without compromising patient privacy [27]. Addressing algorithmic bias, regulatory harmonization, equitable access, and workforce capacity remains essential for realizing inclusive, sustainable AI-integrated cancer medicine [9].

Future advances integrating foundation models, real-time biosensing, and continuous digital biomarker monitoring will enable dynamic, adaptive precision oncology systems serving all populations. Successful translation requires sustained multidisciplinary collaboration, explicit commitment to equity, and alignment of technological development with clinical needs and ethical imperatives, ultimately advancing cancer prevention, early detection, and personalized treatment for all populations.

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