

Foundation Models for Precision Oncology: Integrating Multimodal Cancer Intelligence Across the Clinical Workflow

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ABSTRACT:

Cancer remains one of the leading causes of morbidity and mortality worldwide despite remarkable advances in molecular diagnostics, targeted therapeutics, immunotherapy, and precision medicine. The exponential growth of biomedical data generated from radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory investigations, wearable technologies, and electronic health records has created unprecedented opportunities for artificial intelligence (AI)-driven precision oncology while simultaneously presenting major computational challenges. Foundation models have emerged as a transformative paradigm capable of learning generalized biomedical representations from large-scale multimodal datasets through self-supervised pretraining. Unlike conventional machine learning systems designed for specific clinical tasks, foundation models acquire transferable knowledge that can be adapted across cancer diagnosis, prognostic prediction, molecular characterization, therapeutic optimization, radiogenomics, computational pathology, digital twins, clinical decision support, and personalized medicine. Advances in transformer architectures, multimodal learning, contrastive learning, graph neural networks, large language models, retrieval-augmented generation, agentic AI, and generative artificial intelligence have accelerated development of intelligent oncology foundation models capable of integrating imaging, pathology, multi-omics, longitudinal clinical information, and real-world healthcare data into unified patient-centered computational representations. Despite substantial progress, important challenges remain regarding multimodal data harmonization, computational scalability, explainability, interoperability, cybersecurity, regulatory validation, and equitable implementation. This review provides a comprehensive overview of foundation models in precision oncology, emphasizing computational principles, current clinical applications, implementation challenges, and future perspectives for integrating multimodal cancer intelligence throughout the clinical workflow.[1]

Keywords: Foundation models, Precision oncology, Artificial intelligence, Multimodal learning, Computational oncology, Digital pathology, Medical imaging, Large language models, Clinical decision support, Personalized medicine.

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1. Introduction

Cancer is a biologically heterogeneous disease characterized by genomic instability, epigenetic dysregulation, transcriptional diversity, metabolic reprogramming, immune heterogeneity, and

dynamic interactions between malignant cells and the tumor microenvironment. Although precision oncology has significantly improved patient outcomes through molecular diagnostics and targeted therapies, patients with apparently similar pathological diagnoses frequently exhibit

markedly different therapeutic responses and clinical outcomes because of the extraordinary biological complexity of cancer.[2]

Modern oncology generates enormous quantities of heterogeneous biomedical information through computed tomography, magnetic resonance imaging, positron emission tomography, mammography, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory investigations, wearable biosensors, electronic health records, and longitudinal clinical documentation. While each modality provides valuable insight into tumor biology, conventional artificial intelligence systems frequently analyze these datasets independently, limiting comprehensive patient-level understanding.[3]

Foundation models have emerged as one of the most significant advances in artificial intelligence by enabling generalized representation learning across extremely large biomedical datasets. Rather than performing isolated prediction tasks, foundation models acquire transferable biomedical knowledge through large-scale self-supervised learning that can subsequently be adapted to numerous downstream oncology applications.[4]

The integration of foundation models across the clinical workflow is transforming precision oncology by enabling comprehensive multimodal reasoning that supports diagnosis, molecular characterization, therapeutic planning, disease monitoring, and survivorship care through unified computational intelligence.[5]

2.Evolution of Foundation Models in Oncology

Artificial intelligence in oncology has progressed through several important stages. Early computational systems relied primarily on rule-based algorithms and handcrafted features that provided limited diagnostic support but lacked adaptability. Machine learning subsequently enabled prediction of diagnosis, recurrence, treatment response, toxicity, and survival using structured biomedical datasets.[6]

Deep learning significantly improved computational performance through automated extraction of hierarchical representations from

radiological imaging, digital pathology, genomic sequencing, and physiological signals. Convolutional neural networks revolutionized medical image analysis, whereas recurrent neural networks improved temporal interpretation of longitudinal clinical information.

Transformer architectures introduced self-attention mechanisms capable of efficiently modeling long-range contextual relationships across heterogeneous biomedical modalities. Foundation models extended these capabilities through large-scale self-supervised pretraining on enormous biomedical datasets, enabling generalized representation learning transferable across multiple downstream oncology applications.[7]

Today, multimodal foundation models integrate imaging, pathology, multi-omics, laboratory investigations, electronic health records, wearable technologies, and clinical documentation into comprehensive computational ecosystems capable of supporting the entire precision oncology workflow.[8]

3.Principles of Foundation Models

Foundation models differ fundamentally from conventional artificial intelligence systems because they are pretrained on extremely large multimodal biomedical datasets before adaptation to specialized clinical applications. Rather than learning isolated diagnostic tasks, these models acquire generalized biological, molecular, anatomical, and clinical representations applicable across diverse oncology domains.[9]

Self-supervised learning enables discovery of latent biomedical relationships without requiring extensive manual annotation. Contrastive learning aligns heterogeneous biomedical modalities within shared computational embedding spaces, while transformer architectures provide cross-modal attention mechanisms that integrate imaging, pathology, genomics, laboratory investigations, and clinical narratives into unified patient-specific representations.

Graph neural networks further strengthen biological reasoning by modeling interactions among genes, proteins, signaling pathways, immune networks, therapeutic targets, imaging

biomarkers, and clinical outcomes. These computational principles substantially improve transfer learning, few-shot learning, and zero-shot learning while reducing dependence on manually labeled datasets.[10]

4.Computational Architecture

Foundation model architectures within precision oncology consist of multiple interconnected computational layers responsible for multimodal biomedical data acquisition, preprocessing, representation learning, multimodal fusion, downstream adaptation, and clinical decision support.[11]

The data acquisition layer collects radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory biomarkers, wearable sensor data, medication history, and longitudinal electronic health records. Advanced preprocessing pipelines normalize imaging studies, harmonize molecular datasets, encode clinical narratives through natural language processing, and generate standardized multimodal representations.

Large transformer-based neural networks convert heterogeneous biomedical information into generalized computational embeddings through self-supervised learning. Downstream adaptation modules subsequently fine-tune these embeddings for diagnosis, prognostic prediction, biomarker discovery, therapeutic optimization, toxicity assessment, and survival analysis.

Continuous integration of longitudinal patient information enables adaptive precision oncology by allowing foundation models to evolve alongside individual clinical trajectories.[12]

5.Foundation Models in Medical Imaging

Medical imaging provides one of the richest biomedical domains for foundation model development. Computed tomography, magnetic resonance imaging, positron emission tomography, mammography, ultrasound, and hybrid imaging collectively generate enormous image repositories

suitable for large-scale self-supervised representation learning.[13]

Foundation models pretrained on millions of medical images automatically learn generalized anatomical and pathological representations that can subsequently be adapted to tumor detection, lesion segmentation, disease classification, radiomics, treatment response assessment, and longitudinal disease monitoring.

Compared with conventional convolutional neural networks trained for individual diagnostic tasks, foundation models demonstrate substantially improved robustness, transfer learning, zero-shot learning, and few-shot learning capabilities across multiple cancer types and healthcare environments while requiring fewer annotated datasets.[14]

6.Digital Pathology Foundation Models

Digital pathology has become one of the most important application areas for foundation models because whole-slide imaging generates extremely high-resolution tissue images containing millions of microscopic structures ideally suited for self-supervised learning.[15]

Transformer-based pathology foundation models automatically learn generalized histomorphological representations before adaptation to tumor classification, grading, biomarker prediction, lymph node metastasis detection, recurrence estimation, immune-cell quantification, and survival prediction.

Recent computational studies have demonstrated accurate prediction of clinically relevant biomarkers including EGFR mutations, KRAS mutations, HER2 amplification, microsatellite instability, estrogen receptor status, progesterone receptor status, PD-L1 expression, and numerous additional therapeutic biomarkers directly from routine histopathological images.

Integration of pathology representations with imaging, genomics, laboratory investigations, and longitudinal clinical information substantially improves diagnostic reproducibility while strengthening precision oncology.[16]

7.Multi-Omics Foundation Models

Modern precision oncology increasingly depends upon integration of genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, lipidomics, and single-cell sequencing into comprehensive molecular representations. Foundation models enable generalized learning across these heterogeneous biological modalities through self-supervised transformer architectures and graph neural networks.[17]

Artificial intelligence identifies interactions among genes, proteins, signaling pathways, metabolites, immune responses, and therapeutic targets while supporting molecular subtype classification, biomarker discovery, drug response prediction, systems biology research, and personalized therapeutic planning.

These generalized molecular representations provide increasingly comprehensive understanding of tumor biology while enabling transfer learning across multiple malignancies and healthcare systems.[18]

8.Multimodal Clinical Intelligence

The principal advantage of foundation models lies in their ability to integrate heterogeneous biomedical information throughout the clinical workflow. Radiological imaging, digital pathology, multi-omics, laboratory investigations, wearable technologies, medication history, physician documentation, and longitudinal clinical outcomes are harmonized into unified patient-centered computational representations.[19]

Large multimodal transformer architectures preserve complementary biological information across imaging, pathology, molecular biology, and temporal clinical records while supporting comprehensive reasoning regarding diagnosis, prognosis, therapeutic planning, toxicity assessment, disease monitoring, and survivorship care.

These multimodal computational ecosystems substantially improve individualized clinical decision-making while reducing fragmentation of

information across traditional diagnostic disciplines.[20]

9.Foundation Models for Precision Cancer Diagnosis

One of the most significant clinical applications of foundation models is precision cancer diagnosis through integrated analysis of radiological imaging, digital pathology, multi-omics, laboratory biomarkers, and longitudinal clinical information. Unlike conventional artificial intelligence systems that analyze individual modalities separately, foundation models generate unified patient-specific representations that improve diagnostic reasoning across the entire oncology workflow.[21]

Artificial intelligence combines imaging-derived radiomic features, histopathological characteristics, genomic alterations, transcriptomic signatures, proteomic profiles, laboratory investigations, and clinical documentation to improve tumor detection, molecular subtype classification, disease staging, recurrence prediction, and individualized risk stratification.

These generalized multimodal representations reduce diagnostic variability while supporting multidisciplinary oncology teams through evidence-based computational decision support and more consistent interpretation across diverse healthcare environments.

10.Therapeutic Planning and Personalized Oncology

Foundation models are increasingly transforming precision therapeutics by integrating molecular biology, imaging, pathology, laboratory investigations, treatment history, and patient-specific clinical characteristics into comprehensive computational frameworks capable of supporting individualized treatment planning.[22]

Machine learning algorithms estimate treatment response, progression-free survival, overall survival, recurrence probability, treatment-related toxicity, and mechanisms of therapeutic resistance across chemotherapy, targeted therapy, endocrine

therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment strategies.

Continuous incorporation of updated clinical information enables adaptive therapeutic recommendations that evolve alongside changes in tumor biology and patient health, thereby supporting dynamic precision medicine throughout the clinical workflow.

11.Immunotherapy and Tumor Microenvironment Intelligence

The tumor microenvironment exerts profound influence on disease progression and responsiveness to immunotherapy. Foundation models integrate radiological imaging, computational pathology, transcriptomics, immunomics, spatial biology, laboratory biomarkers, and longitudinal clinical outcomes into unified computational representations of tumor-immune interactions.[23]

Artificial intelligence evaluates tumor-infiltrating lymphocytes, immune checkpoint expression, cytokine signaling pathways, stromal organization, angiogenesis, and immune-cell spatial relationships to estimate responsiveness to immune checkpoint inhibitors, CAR-T cell therapies, cancer vaccines, bispecific antibodies, and adoptive cellular therapies.

By integrating multiple biological modalities, foundation models improve prediction of immunotherapeutic outcomes while supporting increasingly personalized treatment strategies based on each patient's unique immune landscape.

12.Drug Discovery and Clinical Research

Foundation models are accelerating oncology drug discovery by integrating molecular biology, pharmacology, structural biology, systems biology, and real-world clinical outcome data into generalized computational frameworks. Artificial intelligence identifies novel therapeutic targets, predicts drug-target interactions, estimates toxicity profiles, and models mechanisms of therapeutic resistance.[24]

Generative artificial intelligence further enhances pharmaceutical research by designing candidate molecules, predicting protein structures, simulating molecular interactions, and generating synthetic biomedical datasets that accelerate hypothesis generation and preclinical investigation.

Foundation models also improve clinical research by supporting molecular eligibility assessment, patient stratification, adaptive clinical trial optimization, outcome prediction, and identification of patients most likely to benefit from investigational therapies.

13.Digital Twins and Intelligent Clinical Decision Support

The convergence of foundation models with digital twin technology is creating continuously evolving computational representations of individual cancer patients. Digital twins integrate imaging, pathology, multi-omics, wearable biosensors, laboratory investigations, medication history, and longitudinal clinical information into adaptive virtual patient models capable of simulating disease progression and therapeutic response.[25]

Artificial intelligence continuously updates these digital twins as new patient information becomes available, allowing clinicians to evaluate multiple therapeutic strategies before implementation. Foundation models strengthen these systems by providing generalized biomedical reasoning across imaging, molecular biology, pathology, and temporal clinical records.

Within routine oncology practice, intelligent clinical decision-support platforms provide individualized diagnostic assessments, therapeutic recommendations, toxicity predictions, recurrence estimates, and survivorship planning while maintaining physician oversight and multidisciplinary collaboration.

14.Explainability, Trustworthiness, and Clinical Translation

Although foundation models demonstrate remarkable predictive capabilities, successful

clinical implementation requires transparency, interpretability, and clinician trust. Explainable artificial intelligence (XAI) enables healthcare professionals to understand computational reasoning through attention visualization, saliency maps, SHAP (Shapley Additive Explanations), feature attribution analysis, concept attribution, and counterfactual explanations that identify the biological variables contributing most strongly to model predictions.[26]

Several additional challenges remain. Foundation models require large computational resources, standardized multimodal datasets, secure computational infrastructure, interoperability across healthcare systems, prospective multicenter validation, and continuous monitoring for algorithmic bias.

Regulatory approval, cybersecurity, patient privacy, equitable access, and standardized reporting frameworks will remain essential prerequisites for responsible translation into routine precision oncology.

15.Future Perspectives

The future clinical workflow in oncology will likely be driven by increasingly sophisticated multimodal foundation models capable of continuously learning from imaging, pathology, genomics, transcriptomics, proteomics, metabolomics, wearable biosensors, electronic health records, and real-world clinical outcomes.[27]

Emerging technologies including multimodal large language models, agentic artificial intelligence, digital twins, federated learning, reinforcement learning, spatial multi-omics, liquid biopsy, quantum computing, cloud-native healthcare infrastructure, and Internet of Medical Things (IoMT) technologies will substantially expand computational capabilities.

Future foundation models may function as comprehensive biomedical reasoning systems capable of adaptive clinical decision-making, autonomous workflow coordination, personalized patient communication, continuous evidence synthesis, and intelligent healthcare optimization throughout the cancer care continuum.

16.Discussion

Foundation models represent one of the most significant paradigm shifts in computational oncology by enabling generalized artificial intelligence capable of integrating multimodal biomedical information into unified patient-centered computational representations. Unlike conventional task-specific machine learning systems, foundation models acquire transferable biomedical knowledge that supports diagnosis, molecular characterization, prognostic prediction, therapeutic optimization, digital twins, drug discovery, and intelligent clinical decision support across multiple stages of cancer care.[28]

Their ability to generalize across heterogeneous biomedical modalities substantially strengthens precision medicine while reducing fragmentation of clinical information throughout the oncology workflow. Nevertheless, successful implementation requires continued advances in explainable artificial intelligence, computational infrastructure, interoperability, cybersecurity, regulatory science, ethical governance, and international collaboration.

17.Conclusion

Foundation models are redefining precision oncology by enabling generalized artificial intelligence that integrates radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable technologies, electronic health records, and longitudinal clinical information into unified computational frameworks supporting every stage of the clinical workflow.[29]

Advances in transformer architectures, multimodal learning, graph neural networks, large language models, digital twins, federated learning, agentic AI, and generative artificial intelligence are expected to further strengthen these intelligent systems, enabling increasingly accurate diagnosis, adaptive therapeutics, continuous disease monitoring, automated clinical reasoning, and evidence-based decision-making.

Although important scientific, technical, ethical, and regulatory challenges remain, continued interdisciplinary collaboration among oncologists, radiologists, pathologists, molecular biologists, computer scientists, biomedical engineers, healthcare organizations, and regulatory agencies will accelerate responsible clinical translation of foundation models, ultimately improving patient outcomes and advancing the future of precision cancer medicine worldwide.[30]

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