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Large Multimodal Models for Computational Oncology: Opportunities, Challenges, and Clinical Translation

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ABSTRACT

Cancer remains one of the leading causes of morbidity and mortality worldwide despite remarkable advances in molecular biology, precision medicine, targeted therapeutics, and immunotherapy. The rapid expansion of biomedical data generated from radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, electronic health records, laboratory investigations, wearable technologies, and longitudinal clinical documentation has created unprecedented opportunities for computational oncology while simultaneously presenting major analytical challenges. Large multimodal models (LMMs) have emerged as a transformative artificial intelligence (AI) paradigm capable of integrating heterogeneous biomedical information into unified patient-centered representations that support diagnosis, prognostic prediction, molecular characterization, therapeutic optimization, and clinical decision-making. Unlike conventional AI systems designed for single-modality analysis, LMMs combine imaging, pathology, multi-omics, clinical narratives, physiological monitoring, and real-world healthcare data through transformer architectures, multimodal representation learning, self-supervised learning, graph neural networks, retrieval-augmented generation, and foundation model pretraining. These intelligent systems have demonstrated remarkable capabilities across computational pathology, radiogenomics, precision therapeutics, digital twins, clinical trial matching, drug discovery, and survivorship care. Despite substantial advances, significant challenges remain regarding multimodal data harmonization, computational scalability, explainability, interoperability, regulatory validation, cybersecurity, algorithmic fairness, and ethical governance. This review provides a comprehensive overview of large multimodal models in computational oncology, emphasizing computational principles, clinical opportunities, implementation challenges, and future perspectives for translation into routine cancer care.[1]

Keywords: Large multimodal models, Artificial intelligence, Computational oncology, Precision medicine, Digital pathology, Multi-omics, Medical imaging, Foundation models, Clinical decision support, Personalized oncology.

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1. Introduction

Cancer is a highly heterogeneous disease characterized by genomic instability, epigenetic alterations, transcriptional dysregulation, metabolic reprogramming, immune heterogeneity, and continuous interactions between malignant cells and the surrounding tumor microenvironment. Although advances in molecular diagnostics and targeted therapies have

substantially improved patient outcomes, individuals with apparently similar pathological diagnoses frequently exhibit markedly different therapeutic responses and survival outcomes because of the complex biological diversity underlying cancer progression.[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 biomarkers, wearable devices, and electronic health records. While each modality contributes valuable insight into tumor biology, conventional computational approaches often analyze these datasets independently, limiting comprehensive understanding of individual patients.[3]

Artificial intelligence has emerged as one of the most transformative technologies in cancer medicine by enabling automated interpretation of complex biomedical information. More recently, large multimodal models have extended these capabilities by learning unified computational representations across multiple biomedical modalities, enabling comprehensive patient-level reasoning that supports diagnosis, prognosis, therapeutic planning, and adaptive clinical decision-making.[4]

The emergence of large multimodal models therefore represents a major milestone in computational oncology, facilitating increasingly integrated, personalized, and evidence-based precision cancer care through holistic analysis of multimodal biomedical information.[5]

2. Evolution of Large Multimodal Models

Artificial intelligence within oncology has progressed through several major developmental stages. Early computational systems primarily relied on rule-based algorithms and handcrafted features that provided limited diagnostic support but lacked adaptability and generalization. Machine learning subsequently enabled statistical prediction of diagnosis, recurrence, therapeutic response, and survival through structured clinical datasets.[6]

Deep learning revolutionized computational oncology by automatically extracting hierarchical representations from medical imaging and digital pathology. Convolutional neural networks demonstrated remarkable performance across radiology, computational pathology, and image classification, while recurrent neural networks improved temporal analysis of longitudinal clinical information.

Transformer architectures introduced self-attention mechanisms capable of capturing long-range contextual relationships across textual, molecular, and imaging data. Foundation models subsequently enabled generalized representation learning through large-scale self-supervised pretraining, substantially reducing dependence on manually annotated datasets while improving transferability across numerous biomedical tasks.[7]

Recent development of large multimodal models extends these advances by simultaneously integrating imaging, pathology, genomics, multi-omics, laboratory investigations, wearable technologies, and clinical documentation into unified computational frameworks capable of supporting comprehensive precision oncology applications.[8]

3. Computational Principles of Large Multimodal Models

Large multimodal models differ fundamentally from conventional machine learning algorithms because they learn shared computational representations across multiple heterogeneous biomedical modalities rather than independently analyzing individual datasets.[9]

Self-supervised learning enables these models to identify latent biological relationships without requiring extensive manual annotation. Contrastive learning aligns information originating from different modalities by learning common embedding spaces that preserve complementary biological characteristics. Transformer architectures facilitate cross-modal attention mechanisms capable of integrating

radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, laboratory investigations, and clinical narratives into unified patient-level representations.

Graph neural networks further strengthen biological reasoning by modeling interactions among genes, proteins, signaling pathways, metabolic networks, therapeutic targets, and clinical outcomes. Retrieval-augmented generation enables models to access current clinical guidelines, biomedical literature, pharmacological databases, and molecular knowledge before generating evidence-based clinical recommendations.[10]

These computational principles collectively enable large multimodal models to perform increasingly sophisticated reasoning across diverse biomedical domains while supporting comprehensive clinical decision-making.

4. Computational Architecture

Large multimodal oncology models consist of several interconnected computational layers responsible for multimodal data acquisition, preprocessing, representation learning, cross-modal fusion, predictive modeling, and clinical decision support.[11]

The data acquisition layer collects radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, laboratory biomarkers, physiological monitoring, wearable sensor information, medication history, and electronic health records. Advanced preprocessing pipelines subsequently normalize imaging studies, harmonize molecular datasets, encode clinical narratives using natural language processing, align temporal clinical information, and extract quantitative biomedical features.

Large transformer architectures convert heterogeneous biomedical information into shared computational embeddings. Cross-modal fusion mechanisms integrate these embeddings into unified patient-specific representations capable of supporting diagnosis, molecular characterization, therapeutic prediction, toxicity estimation, recurrence assessment, and survival prediction.

Continuous incorporation of longitudinal patient information allows these models to adapt throughout diagnosis, treatment, follow-up, and survivorship, supporting dynamic precision oncology rather than static prediction.[12]

5. Large Multimodal Models in Medical Imaging

Medical imaging provides one of the richest sources of biomedical information within computational oncology. Computed tomography, magnetic resonance imaging, positron emission tomography, mammography, ultrasound, and hybrid imaging collectively generate enormous datasets that are ideally suited for large-scale multimodal representation learning.[13]

Large multimodal models automatically learn generalized anatomical and pathological features from millions of medical images before adapting these representations to downstream oncology tasks including tumor detection, lesion segmentation, disease classification, radiomics, treatment response assessment, and longitudinal disease monitoring.

Unlike conventional imaging algorithms trained for individual diagnostic tasks, multimodal models demonstrate strong transfer learning, few-shot learning, and zero-shot learning capabilities, substantially improving generalizability across healthcare institutions while reducing dependence on manually annotated imaging datasets.[14]

6. Digital Pathology and Computational Histopathology

Digital pathology has become one of the most important applications of large multimodal models because whole-slide imaging generates extremely high-resolution tissue images containing millions of microscopic structures suitable for self-supervised representation learning.[15]

Large pathology foundation models automatically learn generalized histomorphological representations that can

subsequently be adapted to tumor classification, grading, recurrence prediction, biomarker discovery, lymph node metastasis detection, immune-cell quantification, and survival estimation.

Recent computational advances have demonstrated that multimodal pathology models accurately predict clinically relevant molecular biomarkers including EGFR mutations, KRAS mutations, HER2 amplification, microsatellite instability, estrogen receptor status, progesterone receptor status, PD-L1 expression, and additional therapeutic biomarkers directly from routine histopathological images.

Integration of pathology representations with imaging, genomics, and clinical information further strengthens diagnostic precision while improving reproducibility across pathology laboratories.[16]

7. Multi-Omics Integration

Multi-omics technologies—including genomics, transcriptomics, proteomics, metabolomics, epigenomics, lipidomics, immunomics, and single-cell sequencing—provide comprehensive molecular characterization of cancer biology across multiple biological layers. Interpretation of these high-dimensional datasets requires computational approaches capable of modeling complex nonlinear biological relationships.[17]

Large multimodal models integrate heterogeneous omics information using transformer architectures, graph neural networks, biological knowledge graphs, and multimodal representation learning to identify interactions among genes, proteins, signaling pathways, metabolites, immune responses, and therapeutic targets.

These computational approaches facilitate molecular subtype classification, biomarker discovery, therapeutic prediction, drug resistance analysis, and systems biology research while providing increasingly comprehensive understanding of cancer biology beyond individual omics modalities.[18]

8. Longitudinal Clinical Intelligence

Longitudinal clinical information represents an essential component of computational oncology because cancer management extends across diagnosis, treatment, recurrence surveillance, survivorship, and end-of-life care. Electronic health records, physician documentation, laboratory investigations, wearable technologies, medication history, and patient-reported outcomes collectively describe continuously evolving patient trajectories.[19]

Large multimodal models integrate temporal clinical information with imaging, pathology, and molecular biology through temporal transformer architectures and multimodal sequence modeling. These continuously evolving patient representations support prediction of disease progression, treatment adaptation, toxicity, recurrence, and long-term survival while enabling increasingly personalized precision oncology throughout the entire cancer care continuum.[20]

9. Clinical Applications in Precision Oncology

Large multimodal models (LMMs) are increasingly being integrated into routine oncology workflows to support precision diagnosis, prognostic prediction, molecular characterization, therapeutic planning, and longitudinal disease monitoring. By simultaneously analyzing radiological imaging, digital pathology, genomic sequencing, laboratory biomarkers, and clinical documentation, these models provide a comprehensive understanding of individual patient biology that extends beyond conventional single-modality artificial intelligence systems.[21]

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

Such multimodal reasoning supports multidisciplinary oncology teams by generating evidence-based recommendations while reducing diagnostic variability and improving clinical consistency across diverse healthcare settings.

10. Personalized Therapeutics and Treatment Optimization

Personalized treatment planning represents one of the most important clinical applications of large multimodal models. These systems integrate molecular biology, imaging findings, pathology, laboratory biomarkers, treatment history, comorbidities, and longitudinal patient trajectories into unified computational frameworks capable of supporting individualized therapeutic decision-making.[22]

Machine learning algorithms estimate treatment response, recurrence probability, progression-free survival, overall survival, treatment-related toxicity, and mechanisms of acquired resistance across chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment strategies.

Continuous incorporation of updated patient information enables adaptive therapeutic recommendations that evolve alongside changes in tumor biology and patient health, thereby supporting dynamic precision medicine rather than static treatment protocols.

11. Immunotherapy and Tumor Microenvironment Analysis

The tumor microenvironment plays a fundamental role in determining disease progression and responsiveness to immunotherapy. Large multimodal models integrate radiological imaging, computational pathology, transcriptomics, immunomics, spatial biology, laboratory biomarkers, and clinical outcomes to generate comprehensive computational representations of tumor–immune interactions.[23]

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

By integrating multiple biological modalities, these 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 Trial Optimization

Large multimodal models are accelerating oncology drug discovery through integration of molecular biology, structural biology, pharmacology, systems biology, and clinical outcome data into comprehensive computational ecosystems. 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 facilitate hypothesis generation and preclinical research.

Large multimodal models also improve clinical trial efficiency by automating molecular eligibility assessment, patient stratification, endpoint prediction, adaptive trial optimization, and recruitment of patients most likely to benefit from investigational therapies.

13. Digital Twins and Intelligent Clinical Decision Support

The convergence of large multimodal models with digital twin technology is creating continuously evolving computational representations of individual cancer patients. Digital twins integrate radiological 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 virtual models as new clinical information becomes available, allowing clinicians to compare multiple treatment strategies before implementation. Multimodal reasoning strengthens digital twins by providing generalized biomedical knowledge across imaging, molecular biology, pathology, and longitudinal clinical records.

Within routine clinical practice, intelligent decision-support platforms integrate multidisciplinary biomedical information into interactive dashboards that provide individualized diagnostic assessments, prognostic estimates, therapeutic recommendations, toxicity predictions, and survivorship planning while maintaining physician oversight.

14. Explainable Artificial Intelligence and Clinical Translation

Although large multimodal 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, and counterfactual explanations that identify variables contributing to model predictions.[26]

Several additional challenges continue to influence clinical translation. Multimodal biomedical datasets frequently exhibit heterogeneous formats, missing information, institutional variability, and batch effects. Computational infrastructure requirements, algorithmic bias, interoperability limitations, cybersecurity, patient privacy, regulatory approval, and equitable access remain significant barriers to widespread implementation.

Addressing these issues will require standardized biomedical data models, prospective multicenter validation studies, transparent governance frameworks, federated learning strategies, secure computational infrastructure, and international regulatory collaboration.

15. Future Perspectives

Future computational oncology is expected to be increasingly driven by large multimodal 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, digital twins, agentic artificial intelligence, reinforcement learning, spatial transcriptomics, liquid biopsy, single-cell sequencing, quantum computing, federated learning, cloud-native healthcare infrastructure, and Internet of Medical Things (IoMT) technologies will substantially expand computational capabilities.

Future large multimodal models may function as comprehensive biomedical reasoning systems capable of autonomous knowledge synthesis, adaptive therapeutic planning, personalized patient communication, workflow optimization, and continuous evidence generation across global oncology networks.

16. Discussion

Large multimodal models represent one of the most significant technological advances in computational oncology by enabling unified representation learning across medical imaging, digital pathology, multi-omics, laboratory investigations, and longitudinal clinical information. Unlike conventional artificial intelligence systems that analyze individual biomedical modalities independently, these models generate comprehensive patient-specific

representations that support diagnosis, molecular characterization, therapeutic optimization, drug discovery, digital twins, and intelligent clinical decision support.[28]

Their ability to integrate heterogeneous biomedical information offers unprecedented opportunities for precision medicine while reducing fragmentation of clinical decision-making. Nevertheless, successful clinical implementation requires continued advances in explainable artificial intelligence, computational infrastructure, interoperability, cybersecurity, regulatory validation, and equitable deployment across diverse healthcare environments.

17. Conclusion

Large multimodal models are redefining computational oncology by integrating radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable technologies, electronic health records, and longitudinal clinical information into unified computational frameworks capable of supporting precision cancer medicine.[29]

Advances in transformer architectures, self-supervised learning, multimodal foundation models, graph neural networks, retrieval-augmented generation, digital twins, agentic AI, and generative artificial intelligence are expected to further strengthen these intelligent systems, enabling increasingly personalized diagnosis, adaptive therapeutics, continuous disease monitoring, and evidence-based clinical decision-making.

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

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