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EXPLAINABLE MULTIMODAL ARTIFICIAL INTELLIGENCE IN PRECISION ONCOLOGY: FROM BIOMARKER DISCOVERY TO CLINICAL ADOPTION

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Abstract: Explainable multimodal artificial intelligence (XAI) is emerging as a transformative paradigm in precision oncology by combining transparent computational reasoning with comprehensive integration of heterogeneous biomedical data. Although deep learning and foundation artificial intelligence (AI) models have achieved remarkable diagnostic and prognostic performance, their limited interpretability has constrained widespread clinical adoption due to concerns regarding transparency, trust, accountability, and regulatory acceptance. Recent advances in multimodal transformer architectures, graph neural networks, self-supervised learning, reinforcement learning, foundation AI models, and generative artificial intelligence have enabled seamless integration of radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, electronic health records, biomedical literature, and longitudinal clinical outcomes into unified computational representations of cancer biology. Explainable AI techniques including attention visualization, saliency mapping, SHAP (Shapley Additive Explanations), integrated gradients, counterfactual reasoning, uncertainty estimation, concept attribution, and causal inference enable transparent interpretation of multimodal predictions while supporting biomarker discovery, therapeutic optimization, adaptive disease monitoring, digital twin simulation, and evidence-based clinical decision support. Emerging technologies including multimodal large language models, agentic AI, federated learning, retrieval-augmented generation, cancer knowledge graphs, cloud-native healthcare platforms, and digital health ecosystems further strengthen explainable oncology by enabling collaborative, privacy-preserving, trustworthy, and continuously adaptive biomedical intelligence. Despite remarkable technological advances, important scientific, technical, ethical, and regulatory challenges remain regarding multimodal data harmonization, computational scalability, interoperability, algorithmic bias, cybersecurity, clinical validation, and equitable implementation. This review provides a comprehensive overview of explainable multimodal artificial intelligence in precision oncology, emphasizing its role from biomarker discovery to routine clinical adoption.[1]

Keywords: Explainable artificial intelligence, Multimodal AI, Precision oncology, Foundation models, Biomarker discovery, Clinical decision support, Computational oncology, Digital pathology, Radiomics, Personalized medicine.

1. Introduction

Cancer is a biologically complex disease characterized by genomic instability, epigenetic remodeling, transcriptional dysregulation, proteomic adaptation, metabolic reprogramming, immune evasion, stromal remodeling, angiogenesis, and dynamic interactions among malignant cells, immune populations, extracellular matrix, vascular structures, and host physiology. These interconnected biological processes evolve throughout diagnosis, treatment, recurrence, metastasis, and survivorship, making precision oncology increasingly dependent upon computational systems capable of integrating heterogeneous biomedical information while remaining understandable to clinicians.[2]

Modern oncology generates enormous quantities of biomedical information through radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, circulating tumor DNA, wearable physiological monitoring, physician documentation, electronic health records, biomedical literature, and patient-reported outcomes. Although deep learning algorithms demonstrate exceptional predictive performance, their "black-box" characteristics frequently limit clinician trust and hinder translation into routine healthcare.[3]

Explainable multimodal artificial intelligence addresses these limitations by combining transparent computational reasoning with comprehensive integration of multimodal biomedical information, thereby enabling trustworthy precision oncology and evidence-based clinical decision-making.

2. Evolution of Explainable Artificial Intelligence in Oncology

Artificial intelligence in oncology has evolved from conventional statistical learning toward sophisticated multimodal foundation models capable of generalized biomedical reasoning. Early machine learning algorithms frequently relied upon manually engineered features and relatively interpretable statistical models but demonstrated limited predictive performance for complex biomedical data.[4]

Deep learning substantially expanded computational capabilities through automated feature learning from radiological imaging, digital pathology, genomics, and electronic health records. However, increasing model complexity often reduced interpretability, creating challenges regarding transparency, regulatory approval, clinician acceptance, and patient trust.

Recent advances in explainable AI, multimodal transformers, graph neural networks, and foundation models have begun addressing these limitations by integrating high predictive performance with transparent computational reasoning suitable for clinical implementation.[5]

3. Principles of Explainable Multimodal Foundation Models

Foundation AI models differ fundamentally from conventional predictive algorithms because they acquire generalized biomedical representations from massive multimodal datasets before specialization for individual oncology applications. Explainable multimodal AI extends these capabilities by explicitly revealing computational reasoning while integrating heterogeneous biomedical information into interpretable patient-specific representations.[6]

Self-supervised learning enables discovery of latent biological relationships without requiring extensive manual annotation, while multimodal transformer architectures align radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, laboratory biomarkers, wearable physiological monitoring, physician documentation, patient-reported outcomes, biomedical literature, and longitudinal clinical trajectories within unified computational embedding spaces.

Graph neural networks further characterize interactions among genes, proteins, signaling pathways, metabolites, immune populations, imaging phenotypes, tissue architecture, therapeutic targets, physiological variables, environmental exposures, and clinical outcomes, while explainability algorithms identify the biological mechanisms underlying computational predictions.[7]

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4. Computational Architecture

Modern explainable multimodal oncology platforms consist of interconnected computational layers responsible for biomedical data acquisition, preprocessing, multimodal representation learning, explainable inference, graph reasoning, predictive analytics, digital twin simulation, knowledge integration, uncertainty estimation, and intelligent clinical decision support.[8]

The acquisition layer continuously integrates radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, circulating tumor DNA, physician documentation, wearable physiological monitoring, biomedical literature, pharmacological databases, clinical guidelines, and electronic health records. Advanced preprocessing pipelines normalize imaging studies, harmonize molecular datasets, encode biomedical narratives using natural language processing, synchronize temporal patient information, and continuously incorporate emerging scientific evidence.

Foundation AI models subsequently generate generalized multimodal embeddings representing molecular biology, tissue architecture, imaging phenotypes, physiological function, environmental exposures, and longitudinal clinical trajectories while simultaneously producing interpretable explanations supporting clinician understanding and evidence-based reasoning.[9]

5. Explainable AI for Biomarker Discovery

One of the most important applications of explainable multimodal AI is biomarker discovery through transparent identification of clinically meaningful biological features. Foundation AI models integrate radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, laboratory biomarkers, and longitudinal clinical outcomes into generalized molecular representations capable of identifying latent biological relationships associated with diagnosis, prognosis, therapeutic response, and survival.[10]

Explainability techniques including SHAP values, integrated gradients, attention visualization, feature attribution analysis, and saliency mapping reveal the imaging characteristics, molecular alterations, histopathological structures, and physiological variables contributing to computational predictions. Rather than generating opaque outputs, these methods provide biologically interpretable evidence supporting biomarker validation and translational research.

These computational advances substantially accelerate biomarker discovery while strengthening biological understanding and clinical confidence.[11]

6. Multimodal Data Integration

Comprehensive characterization of cancer biology requires seamless integration of complementary biomedical modalities including radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, microbiomics, single-cell sequencing, spatial biology, laboratory biomarkers, and wearable physiological monitoring. Foundation AI models harmonize these diverse information sources using multimodal transformers and graph neural networks capable of generating generalized representations of evolving tumor biology.[12]

Explainable AI enables visualization of cross-modal relationships among imaging phenotypes, histopathological architecture, molecular pathways, immune responses, physiological monitoring, and clinical outcomes, thereby improving understanding of multimodal computational reasoning.

These integrated and interpretable representations substantially improve diagnosis, prognostic prediction, therapeutic optimization, biomarker discovery, precision immunotherapy, adaptive therapeutics, and translational cancer research.[13]

7. Explainable Clinical Decision Support

Successful implementation of artificial intelligence in oncology depends upon transparent clinical decision support that complements physician expertise rather than replacing clinical judgment. Explainable multimodal AI synthesizes radiological imaging, digital pathology, molecular diagnostics, laboratory investigations, physician documentation, biomedical literature, clinical guidelines, and longitudinal patient information

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into interpretable recommendations supporting multidisciplinary oncology practice.[14]
Interactive explanations identify the biological variables responsible for diagnostic classifications, therapeutic prioritization, toxicity estimation, recurrence prediction, and survival forecasting while simultaneously quantifying model uncertainty and confidence. Clinicians can therefore critically evaluate computational reasoning before integrating AI recommendations into individualized patient care.
Explainable decision support substantially improves clinician confidence, workflow efficiency, regulatory compliance, and patient-centered precision oncology.[15]

8. Digital Health and Continuous Explainable Monitoring

Digital health technologies including wearable biosensors, mobile health applications, remote physiological monitoring, smart medical devices, patient-reported outcomes, and Internet of Medical Things (IoMT) platforms continuously generate longitudinal physiological information throughout the cancer care continuum. Explainable AI integrates these digital biomarkers with laboratory investigations, molecular biology, radiological imaging, digital pathology, medication adherence, and electronic health records while transparently identifying physiological variables associated with treatment response, toxicity, disease progression, and survivorship.[16]
Continuous explainable monitoring enables clinicians to understand why specific alerts are generated, improving trust, reducing alarm fatigue, supporting early intervention, and strengthening personalized supportive care.
Digital health therefore represents an indispensable component of trustworthy multimodal oncology ecosystems.[17]

9. Trustworthy Multimodal Clinical Intelligence

One of the greatest strengths of explainable multimodal foundation models is their ability to unify radiology, pathology, multi-omics, laboratory biomarkers, biomedical literature, pharmacological knowledge, wearable physiological monitoring, electronic health records, patient-reported outcomes, and longitudinal clinical trajectories into transparent patient-specific computational representations. Rather than generating unexplained predictions, these systems reveal the biological rationale underlying diagnostic classifications, biomarker discovery, therapeutic optimization, disease monitoring, recurrence prediction, survival estimation, and multidisciplinary clinical decision-making. This transparent multimodal intelligence establishes the computational foundation for trustworthy precision oncology, digital twins, adaptive therapeutics, evidence-based clinical decision support, and responsible clinical adoption of artificial intelligence throughout the cancer care continuum.[18][19][20]

10. Digital Twins and Explainable Virtual Patient Modeling

Digital twin technology represents one of the most transformative applications of explainable multimodal artificial intelligence by creating continuously evolving virtual representations of individual cancer patients synchronized with their biological counterparts. Foundation AI models integrate serial radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, medication history, patient-reported outcomes, and longitudinal clinical information into adaptive computational patient models capable of simulating disease progression, therapeutic response, treatment-related toxicity, recurrence, metastatic dissemination, and survival.[21]
Unlike conventional predictive models that generate opaque recommendations, explainable digital twins continuously update their computational representations while revealing the biological rationale underlying simulated outcomes. Integration of multimodal molecular biology with interpretable predictive simulation enables virtual patients to evaluate alternative therapeutic strategies, optimize treatment sequencing, anticipate mechanisms of therapeutic resistance, personalize supportive care, and estimate long-term clinical outcomes according to evolving patient biology. Clinicians can therefore understand not only the predicted outcome but

also the imaging, molecular, pathological, physiological, and clinical factors driving computational recommendations.

By combining transparent multimodal intelligence with predictive simulation, explainable digital twins bridge computational reasoning and individualized clinical decision-making.

11. Intelligent Explainable Clinical Decision Support

Explainable multimodal AI provides the computational infrastructure for next-generation clinical decision-support systems capable of integrating heterogeneous biomedical information into transparent patient-centered recommendations. Rather than independently interpreting radiological imaging, digital pathology, molecular diagnostics, laboratory investigations, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and evidence-based clinical guidelines, these systems synthesize diverse biomedical information into unified computational representations while explicitly identifying the evidence supporting each recommendation.[22]

Interactive clinical dashboards generate individualized diagnostic summaries, molecular biomarker analyses, radiomic and pathomic interpretations, digital twin simulations, therapeutic recommendations, toxicity estimates, recurrence probabilities, disease progression forecasts, survival predictions, uncertainty scores, and longitudinal treatment response assessments while facilitating collaboration among oncologists, radiologists, pathologists, surgeons, radiation oncologists, molecular biologists, pharmacists, nurses, genetic counselors, biomedical engineers, computational scientists, and healthcare administrators.

These transparent clinical intelligence systems improve workflow efficiency, strengthen multidisciplinary communication, enhance clinician confidence, reduce fragmentation of biomedical information, and promote evidence-based personalized cancer management.

12. Continuous Learning and Adaptive Explainability

A defining characteristic of explainable multimodal AI is the ability to continuously evolve as new biomedical information becomes available while maintaining transparent computational reasoning. Artificial intelligence incorporates serial imaging examinations, computational pathology, circulating tumor DNA, laboratory biomarkers, wearable physiological monitoring, medication adherence, patient-reported outcomes, biomedical literature, pharmacological evidence, clinical guidelines, and real-world treatment outcomes into adaptive computational frameworks capable of continuously refining predictive accuracy throughout the patient's clinical journey.[23]

Continual learning algorithms enable incremental refinement of computational knowledge without catastrophic forgetting, while reinforcement learning optimizes biomarker interpretation, therapeutic prioritization, disease monitoring, toxicity prediction, and supportive care through iterative evaluation of longitudinal patient outcomes. Explainability algorithms simultaneously adapt to evolving knowledge, ensuring that biological reasoning remains interpretable as computational models improve.

This adaptive computational paradigm transforms oncology into a continuously learning healthcare ecosystem capable of rapidly translating scientific discoveries into transparent individualized clinical practice.

13. Federated Explainable AI Networks

Development of highly generalizable explainable foundation AI models requires access to diverse biomedical datasets representing multiple healthcare systems, imaging platforms, pathology laboratories, molecular technologies, wearable ecosystems, treatment protocols, and patient populations. Federated learning enables collaborative development of explainable multimodal intelligence while preserving patient privacy and institutional governance through decentralized computational training.[24]

Participating healthcare institutions independently train local models using radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory

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investigations, wearable monitoring, liquid biopsy, electronic health records, biomedical literature, and longitudinal clinical records while securely exchanging encrypted model parameters rather than identifiable patient information. Transparent explanation modules accompany predictive outputs, allowing external validation of biological reasoning across institutions.

Federated explainable AI ecosystems therefore establish international computational oncology networks capable of accelerating scientific discovery, improving equitable access to precision medicine, reducing institutional bias, and supporting global cancer research while maintaining responsible biomedical data stewardship.

14. Validation, Ethical Governance, and Regulatory Readiness

Successful implementation of explainable multimodal artificial intelligence requires transparent, interpretable, reproducible, and rigorously validated computational systems capable of supporting clinician confidence, patient trust, regulatory approval, and healthcare accountability. Explainable AI enables clinicians to understand computational reasoning through attention visualization, saliency maps, SHAP (Shapley Additive Explanations), integrated gradients, feature attribution analysis, uncertainty estimation, confidence calibration, concept attribution, multimodal attention mapping, and counterfactual explanations identifying the imaging, molecular, pathological, physiological, pharmacological, and clinical variables responsible for predictive outputs.[25]

Clinical deployment additionally requires standardized multimodal datasets, interoperable computational infrastructure, prospective multicenter validation, external benchmarking, cybersecurity safeguards, continuous monitoring for algorithmic bias, transparent reporting standards, explainability benchmarking, and compliance with evolving international regulatory frameworks governing AI-enabled healthcare technologies.

Responsible implementation further depends upon patient privacy, informed consent, transparency, accountability, fairness, equitable access, responsible data governance, continuous post-deployment surveillance, clinician education, and multidisciplinary oversight to ensure trustworthy integration of explainable artificial intelligence into routine oncology practice.

15. Future Perspectives

Future explainable multimodal oncology ecosystems will increasingly integrate foundation models, multimodal large language models, agentic artificial intelligence, graph neural networks, reinforcement learning, federated learning, digital twins, spatial multi-omics, single-cell sequencing, liquid biopsy, quantum computing, Internet of Medical Things (IoMT), cloud-native healthcare infrastructure, biomedical knowledge graphs, retrieval-augmented generation, causal artificial intelligence, and autonomous reasoning systems into unified precision oncology platforms.[26]

These next-generation computational ecosystems will continuously integrate molecular biology, radiological imaging, digital pathology, laboratory medicine, wearable physiological monitoring, environmental exposures, electronic health records, biomedical literature, pharmacological databases, global clinical guidelines, and real-world clinical outcomes while autonomously generating transparent diagnostic explanations, biomarker interpretations, therapeutic recommendations, adaptive clinical trial strategies, personalized survivorship plans, and continuously synthesized biomedical evidence.

Such explainable multimodal intelligence ecosystems are expected to transform oncology from opaque algorithmic prediction toward transparent, adaptive, trustworthy, and precision-guided cancer care.

16. Discussion

Explainable multimodal artificial intelligence represents one of the most significant paradigm shifts in computational oncology by integrating radiology, pathology, multi-omics, laboratory biomarkers, wearable health technologies, biomedical literature, pharmacological knowledge, digital biomarkers, digital twins, and foundation AI models into transparent computational ecosystems capable of supporting comprehensive personalized cancer care. Unlike conventional "black-box" algorithms that generate

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predictions without biological interpretation, explainable AI continuously synthesizes heterogeneous molecular, imaging, pathological, physiological, and clinical information while revealing the computational reasoning supporting individualized recommendations.[27]

Applications spanning computational pathology, radiogenomics, biomarker discovery, digital twins, precision immunotherapy, adaptive therapeutics, remote patient monitoring, federated collaboration, digital health, survivorship management, intelligent clinical decision support, and translational research demonstrate the extraordinary potential of explainable multimodal AI to redefine future oncology. Nevertheless, successful implementation requires continued advances in multimodal data harmonization, explainability science, interoperability, computational infrastructure, cybersecurity, regulatory science, ethical governance, clinician education, and sustained multidisciplinary collaboration.

As biomedical knowledge and healthcare data continue to expand exponentially, explainable multimodal artificial intelligence is expected to become one of the foundational computational infrastructures supporting trustworthy precision oncology worldwide.

17. Conclusion

Explainable multimodal artificial intelligence is transforming precision oncology by integrating radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable health technologies, biomedical literature, electronic health records, digital biomarkers, digital twins, and foundation AI models into transparent computational ecosystems capable of supporting biomarker discovery, prognostic prediction, therapeutic optimization, adaptive disease monitoring, personalized cancer treatment, and evidence-based clinical decision-making throughout the cancer care continuum.[28]

Advances in multimodal transformer architectures, graph neural networks, self-supervised learning, federated learning, reinforcement learning, multimodal large language models, explainable artificial intelligence, agentic AI, digital twins, retrieval-augmented generation, and generative artificial intelligence are expected to further strengthen trustworthy oncology ecosystems, enabling increasingly accurate molecular characterization, transparent clinical reasoning, adaptive therapeutics, continuous disease surveillance, and responsible clinical adoption of artificial intelligence.[29]

Although important scientific, technical, ethical, regulatory, and implementation challenges remain, sustained collaboration among oncologists, radiologists, pathologists, molecular biologists, biomedical engineers, computer scientists, healthcare organizations, policymakers, industry partners, patients, and regulatory agencies will accelerate the responsible implementation of explainable multimodal AI. These innovations have the potential to improve patient outcomes, enhance healthcare efficiency, strengthen clinician trust, reduce disparities in cancer care, accelerate translational research, and establish a new era of transparent, adaptive, trustworthy, and continuously learning precision oncology worldwide.[30]

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