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NEXT-GENERATION AI IN ONCOLOGY: EXPLAINABLE FOUNDATION MODELS FOR PRECISION DIAGNOSIS, PROGNOSIS, AND TREATMENT OPTIMIZATION

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Abstract: Artificial intelligence (AI) is reshaping modern oncology through the emergence of explainable foundation models capable of integrating heterogeneous biomedical information into intelligent computational ecosystems that support precision diagnosis, prognostic prediction, and individualized therapeutic optimization. Conventional machine learning algorithms have demonstrated remarkable performance in isolated oncology applications; however, their task-specific design, limited interpretability, and dependence on fragmented datasets restrict their widespread clinical implementation. Recent advances in foundation AI models, multimodal transformer architectures, graph neural networks, self-supervised learning, and generative artificial intelligence have enabled generalized biomedical representation learning across radiological imaging, digital pathology, genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory biomarkers, circulating tumor DNA, wearable physiological monitoring, electronic health records, and longitudinal clinical outcomes. These intelligent computational systems support early cancer detection, molecular characterization, biomarker discovery, prognostic prediction, therapeutic optimization, immunotherapy selection, digital twin simulation, adaptive disease monitoring, and evidence-based clinical decision support. Explainable artificial intelligence (XAI) techniques—including attention visualization, saliency mapping, feature attribution, SHAP (Shapley Additive Explanations), counterfactual reasoning, and uncertainty estimation—provide transparency necessary for clinician confidence, regulatory approval, and trustworthy deployment. Emerging technologies including multimodal large language models, federated learning, reinforcement learning, retrieval-augmented generation, and agentic AI further strengthen explainable computational oncology through collaborative, privacy-preserving, and continuously adaptive biomedical intelligence. Despite substantial technological progress, important scientific, technical, ethical, and regulatory challenges remain regarding multimodal data harmonization, computational scalability, interoperability, explainability, cybersecurity, clinical validation, and equitable implementation. This review provides a comprehensive overview of next-generation explainable foundation AI models for precision diagnosis, prognosis, and treatment optimization in modern oncology.[1]

Keywords: *Explainable artificial intelligence, Foundation models, Precision oncology, Computational oncology, Digital pathology, Radiomics, Multi-omics, Clinical decision support, Personalized medicine, Cancer diagnosis.*

1. Introduction

Cancer is a biologically dynamic disease characterized by continuous genomic evolution, epigenetic remodeling, immune adaptation, metabolic reprogramming, angiogenesis, tissue remodeling, and intricate interactions among malignant cells, stromal components, immune populations, and host physiology. These interconnected biological processes evolve throughout diagnosis, treatment, recurrence, metastasis, and survivorship, making precision oncology increasingly dependent upon

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computational systems capable of integrating heterogeneous biomedical information across multiple biological scales.[2]

Modern oncology routinely generates enormous quantities of biomedical data 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, and patient-reported outcomes. Although each modality contributes valuable biological insight, isolated interpretation frequently overlooks systems-level relationships governing disease progression, therapeutic response, resistance mechanisms, and long-term clinical outcomes.[3]

Artificial intelligence has emerged as a transformative computational technology capable of integrating these heterogeneous biomedical datasets into unified patient-centered representations. Foundation AI models extend these capabilities through generalized multimodal learning while explainable artificial intelligence provides transparent computational reasoning essential for responsible clinical translation.

The convergence of explainable AI and foundation models therefore establishes a transformative framework for trustworthy precision oncology.[4]

2. Evolution of Explainable AI in Oncology

Artificial intelligence in oncology has evolved from conventional statistical analyses toward intelligent computational ecosystems capable of continuously learning from diverse biomedical data. Early machine learning algorithms relied primarily upon handcrafted feature engineering and task-specific predictive models developed for isolated diagnostic or prognostic applications. Although these systems demonstrated important clinical value, they frequently operated as opaque "black-box" algorithms with limited interpretability.[5]

Deep learning substantially expanded computational capabilities through automated representation learning from radiological imaging, digital pathology, genomic sequencing, and electronic health records. Transformer architectures further revolutionized biomedical artificial intelligence by enabling generalized contextual learning across heterogeneous biomedical modalities.

Foundation AI models now acquire transferable biomedical knowledge through large-scale self-supervised pretraining, while explainable artificial intelligence techniques increasingly provide transparent visualization of computational reasoning, enabling clinician trust, regulatory acceptance, and responsible implementation.[6]

3. Principles of Explainable Foundation Models

Explainable foundation AI models differ fundamentally from conventional artificial intelligence because they simultaneously learn generalized biomedical representations and provide interpretable computational reasoning supporting clinical decision-making. Rather than functioning as isolated predictive algorithms, these systems develop transferable computational knowledge applicable across diagnosis, prognosis, molecular characterization, biomarker discovery, therapeutic optimization, disease monitoring, computational pathology, radiomics, and intelligent clinical decision support.[7]

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, laboratory biomarkers, wearable physiological monitoring, physician documentation, patient-reported outcomes, and longitudinal clinical trajectories within unified computational embedding spaces.

Graph neural networks further characterize interactions among genes, proteins, signaling pathways, immune populations, imaging phenotypes, tissue architecture, therapeutic targets, physiological variables, and clinical outcomes, thereby enabling systems-level computational reasoning supporting precision oncology.[8]

4. Computational Architecture

Modern explainable foundation model platforms consist of interconnected computational layers

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responsible for biomedical data acquisition, preprocessing, representation learning, multimodal fusion, explainability analysis, adaptive learning, predictive analytics, digital twin simulation, and intelligent clinical decision support.[9]

The acquisition layer continuously integrates radiological imaging, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, circulating tumor DNA, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and electronic health records. Advanced preprocessing pipelines normalize imaging studies, harmonize molecular datasets, encode clinical narratives using natural language processing, and synchronize temporal patient information.

Foundation AI models subsequently generate generalized multimodal embeddings representing molecular biology, tissue architecture, imaging phenotypes, physiological function, and longitudinal clinical trajectories. Explainability modules provide transparent interpretation of these representations while supporting trustworthy clinical translation.[10]

5. Explainable AI for Precision Diagnosis

Early and accurate diagnosis remains one of the most important determinants of successful cancer treatment. Explainable foundation AI models substantially improve diagnostic accuracy by integrating radiological imaging, digital pathology, laboratory biomarkers, circulating tumor DNA, genomic profiling, and electronic health records into unified computational frameworks capable of identifying subtle biological abnormalities associated with early tumorigenesis.[11]

Unlike conventional black-box algorithms, explainable AI systems generate attention maps, saliency visualizations, feature attribution analyses, uncertainty estimates, and counterfactual explanations demonstrating why specific imaging regions, histopathological structures, molecular biomarkers, or clinical variables contributed to diagnostic predictions.

These transparent computational explanations strengthen clinician confidence while improving reproducibility, accountability, and adoption of AI-assisted cancer diagnosis.[12]

6. Explainable Molecular Intelligence

Comprehensive molecular characterization represents one of the greatest strengths of explainable foundation AI models. Artificial intelligence integrates genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, microbiomics, spatial biology, and single-cell sequencing into generalized molecular representations capable of characterizing evolving tumor biology across multiple organizational scales.[13]

Transformer architectures identify latent biological relationships among genes, proteins, signaling pathways, metabolites, immune responses, and therapeutic targets, while graph neural networks model complex biological interaction networks supporting systems-level computational reasoning. Explainability methods further identify the molecular pathways, biomarkers, and biological mechanisms responsible for predictive outputs.

These transparent molecular representations facilitate biomarker discovery, molecular subtype classification, therapeutic response prediction, and translational oncology research.[14]

7. Explainable Radiomics and Digital Pathology

Radiological imaging and digital pathology provide complementary information describing cancer biology across macroscopic and microscopic organizational scales. Foundation AI models automatically extract generalized radiomic and pathomic representations from computed tomography, magnetic resonance imaging, positron emission tomography, ultrasound, and whole-slide pathology images without requiring handcrafted feature engineering.[15]

Explainable artificial intelligence highlights image regions, tissue structures, immune infiltration patterns, angiogenesis, fibrosis, necrosis, and cellular morphology that contribute to computational predictions. These visual explanations facilitate verification by radiologists

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and pathologists while strengthening confidence in AI-supported diagnostic interpretation.

Integration of explainable imaging intelligence with molecular biology substantially improves diagnosis, prognostic prediction, biomarker discovery, therapeutic optimization, and longitudinal disease monitoring.[16]

8. Clinical Intelligence Through Electronic Health Records

Electronic health records provide one of the richest longitudinal sources of clinical intelligence available in oncology. Structured laboratory investigations, medication history, pathology reports, treatment timelines, physician documentation, hospitalizations, patient-reported outcomes, and survivorship information collectively provide comprehensive patient-level context extending beyond molecular diagnostics.[17]

Foundation AI models employ natural language processing, temporal transformers, and multimodal reasoning architectures to integrate structured and unstructured EHR data with radiological imaging, digital pathology, molecular biology, laboratory biomarkers, and physiological monitoring into unified patient-specific computational representations. Explainability methods identify the clinical variables, laboratory findings, medications, and historical events contributing to individualized predictions.

These transparent clinical embeddings substantially improve prognostic prediction, toxicity estimation, therapeutic optimization, recurrence surveillance, and evidence-based clinical decision-making.[18]

9. Explainable Therapeutic Optimization

One of the most clinically important applications of explainable foundation AI models is individualized therapeutic optimization through comprehensive integration of molecular biology, imaging phenotypes, histopathological characteristics, laboratory biomarkers, wearable physiological monitoring, medication history, and longitudinal clinical trajectories. These intelligent systems predict responsiveness to chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment combinations while simultaneously providing interpretable explanations identifying the biological, imaging, molecular, and clinical evidence supporting each recommendation. This transparent decision-making framework strengthens clinician confidence, facilitates multidisciplinary treatment planning, and accelerates responsible implementation of precision oncology in routine clinical practice.[19][20]

10. Digital Twins and Explainable Virtual Patient Modeling

Digital twin technology represents one of the most transformative applications of explainable foundation AI models 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, 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, digital twins continuously update their computational representations as new biomedical information becomes available. Explainable AI modules provide transparent visualization of the molecular pathways, imaging biomarkers, histopathological features, physiological parameters, and clinical variables influencing each simulation. These interpretable virtual patients enable clinicians to evaluate multiple therapeutic strategies before implementation while understanding the computational reasoning underlying each recommendation.

By combining multimodal biomedical intelligence with transparent predictive simulation, digital twins transform computational oncology from retrospective analysis toward trustworthy precision medicine.

11. Intelligent Clinical Decision Support

Explainable foundation AI models provide the computational infrastructure for next-generation clinical decision-support systems capable of integrating heterogeneous biomedical information into comprehensive patient-centered recommendations. Rather than interpreting radiological imaging, digital pathology, molecular diagnostics, laboratory investigations, wearable physiological monitoring, medication history, physician documentation, patient-reported outcomes, and evidence-based clinical guidelines independently, these models synthesize diverse biomedical information into unified computational representations supporting multidisciplinary oncology practice.[22]

Interactive clinical dashboards generate individualized diagnostic summaries, multimodal biomarker analyses, digital twin simulations, therapeutic recommendations, toxicity estimates, recurrence probabilities, disease progression forecasts, and survival predictions while simultaneously presenting interpretable explanations supporting each prediction. These transparent systems facilitate collaboration among oncologists, radiologists, pathologists, surgeons, radiation oncologists, molecular biologists, pharmacists, nurses, genetic counselors, and computational scientists while improving workflow efficiency and evidence-based clinical decision-making.

12. Continuous Learning and Adaptive Explainable Intelligence

A defining characteristic of next-generation explainable foundation AI models is their 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, and real-world clinical evidence 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 of previously acquired information, while reinforcement learning optimizes therapeutic recommendations through iterative evaluation of treatment outcomes. Explainability modules simultaneously monitor evolving computational reasoning, enabling clinicians to understand how newly acquired biomedical evidence modifies individualized predictions.

This adaptive computational paradigm transforms oncology into a continuously learning healthcare ecosystem capable of supporting trustworthy real-time precision medicine.

13. Federated Explainable Foundation Model 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, treatment protocols, and patient populations. Federated learning enables collaborative development of foundation AI models while preserving patient privacy and institutional governance through decentralized computational training.[24]

Participating healthcare institutions independently train local explainable models using radiological imaging, digital pathology, genomics, transcriptomics, laboratory investigations, wearable monitoring, liquid biopsy, electronic health records, and longitudinal clinical records while securely exchanging encrypted model parameters rather than identifiable patient information. This collaborative learning strategy substantially improves algorithm robustness, fairness, external validity, transparency, and generalizability across diverse healthcare environments.

Federated explainable AI ecosystems therefore establish international computational oncology networks capable of accelerating scientific discovery while maintaining responsible biomedical data stewardship.

14. Validation, Regulation, and Ethical Governance

Successful implementation of explainable foundation AI models requires transparent, reproducible, rigorously validated, and clinically trustworthy computational systems capable of supporting clinician confidence, patient trust, and regulatory approval. Explainable artificial intelligence employs attention visualization, saliency maps, SHAP (Shapley Additive Explanations), feature attribution analysis, uncertainty estimation, local interpretable explanations, and counterfactual reasoning to identify the imaging, molecular, pathological, physiological, 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, and compliance with evolving international regulatory frameworks governing AI-enabled healthcare technologies.

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

15. Future Perspectives

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

These next-generation computational ecosystems will continuously integrate molecular biology, imaging, pathology, laboratory medicine, wearable physiological monitoring, environmental exposures, electronic health records, biomedical literature, and real-world clinical outcomes while autonomously coordinating diagnostic workflows, optimizing therapeutic strategies, supporting adaptive clinical trials, generating personalized patient communication, and continuously synthesizing biomedical evidence.

Equally important, future systems will provide increasingly sophisticated explanations supporting every stage of clinical reasoning, thereby strengthening clinician trust and facilitating responsible global implementation.

16. Discussion

Explainable foundation AI models represent one of the most significant paradigm shifts in computational oncology by integrating molecular biology, radiological imaging, digital pathology, laboratory biomarkers, wearable technologies, digital twins, and longitudinal clinical intelligence into transparent computational ecosystems capable of supporting comprehensive personalized cancer care. Unlike conventional black-box artificial intelligence systems developed for isolated predictive tasks, these intelligent frameworks simultaneously analyze multimodal biomedical information while providing interpretable computational reasoning supporting individualized clinical decisions.[27]

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

As biomedical knowledge and healthcare data continue to expand exponentially, explainable foundation AI models are expected to become the cornerstone of trustworthy precision oncology worldwide.

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17. Conclusion

Next-generation explainable foundation AI models are transforming precision oncology by integrating radiological imaging, digital pathology, multi-omics, laboratory biomarkers, wearable technologies, electronic health records, digital twins, and longitudinal clinical intelligence into transparent computational ecosystems capable of supporting accurate diagnosis, biomarker discovery, prognostic prediction, therapeutic optimization, adaptive disease monitoring, and individualized clinical decision-making throughout the cancer care continuum.[28]

Advances in transformer architectures, multimodal learning, graph neural networks, self-supervised learning, federated learning, reinforcement learning, digital twins, multimodal large language models, agentic AI, and generative artificial intelligence are expected to further strengthen explainable oncology ecosystems, enabling increasingly accurate molecular characterization, predictive clinical intelligence, adaptive therapeutics, continuous disease surveillance, and continuously personalized cancer care while maintaining transparency and clinical trust.[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, and regulatory agencies will accelerate the responsible implementation of explainable foundation AI models. These innovations have the potential to improve patient outcomes, enhance healthcare efficiency, reduce disparities in cancer care, accelerate translational research, and establish a new era of intelligent, transparent, adaptive, and continuously learning precision oncology worldwide.[30]

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