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AI-ENABLED PRECISION RADIOPATHOMICS: INTEGRATING IMAGING, HISTOPATHOLOGY, AND GENOMICS FOR PERSONALIZED CANCER CARE

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Abstract: Artificial intelligence (AI)-enabled precision radiopathomics has emerged as a transformative paradigm in precision oncology by integrating radiological imaging, digital histopathology, genomics, and multimodal biomedical data into unified computational frameworks for personalized cancer care. Conventional oncology frequently analyzes imaging, pathology, and molecular biomarkers independently, limiting comprehensive understanding of tumor heterogeneity, molecular evolution, therapeutic responsiveness, and disease progression. Recent advances in foundation AI models, multimodal transformer architectures, graph neural networks, self-supervised learning, reinforcement learning, and generative artificial intelligence have enabled seamless integration of computed tomography, magnetic resonance imaging, positron emission tomography, ultrasound, 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. These intelligent systems support precision diagnosis, biomarker discovery, molecular characterization, prognostic prediction, therapeutic optimization, digital twin simulation, adaptive disease monitoring, and evidence-based clinical decision support. Emerging technologies including multimodal large language models, federated learning, retrieval-augmented generation, explainable artificial intelligence, agentic AI, cloud-native healthcare platforms, cancer knowledge graphs, and digital health ecosystems further strengthen radiopathomics by enabling collaborative, privacy-preserving, transparent, and continuously adaptive biomedical intelligence. Despite remarkable technological progress, important scientific, technical, ethical, and regulatory challenges remain regarding multimodal data harmonization, computational scalability, interoperability, cybersecurity, clinical validation, regulatory acceptance, and equitable implementation. This review provides a comprehensive overview of AI-enabled precision radiopathomics, emphasizing integration of imaging, histopathology, and genomics for personalized cancer care.[1]

Keywords: *Radiopathomics, Foundation models, Artificial intelligence, Precision oncology, Digital pathology, Radiomics, Genomics, Computational oncology, Personalized medicine, Multimodal learning.*

1. Introduction

Cancer is a biologically heterogeneous disease characterized by genomic instability, epigenetic remodeling, immune adaptation, metabolic reprogramming, angiogenesis, stromal remodeling, 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, requiring computational systems capable of integrating heterogeneous biomedical information across multiple biological scales.[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 each modality contributes

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valuable biological insight, isolated interpretation frequently limits comprehensive characterization of tumor biology and individualized therapeutic decision-making.[3]

Radiopathomics addresses these limitations by integrating imaging phenotypes, histopathological architecture, molecular biology, and clinical information through foundation AI models, thereby enabling comprehensive characterization of tumor heterogeneity and precision oncology.

2. Evolution of Radiopathomics

Radiopathomics has evolved from independent analyses of radiological imaging and histopathology toward intelligent multimodal computational ecosystems capable of integrating imaging, pathology, and molecular biology into unified patient-specific representations. Early radiomics studies focused primarily on quantitative imaging biomarkers, while digital pathology independently characterized microscopic tissue architecture. Although both approaches generated valuable biological information, limited cross-modal integration constrained comprehensive understanding of tumor biology.[4]

Deep learning substantially expanded computational capabilities by enabling automated feature learning from radiological imaging, digital pathology, genomics, and electronic health records. Transformer architectures subsequently revolutionized biomedical artificial intelligence by enabling contextual learning across heterogeneous biomedical modalities.

Foundation AI models now acquire transferable biomedical knowledge through large-scale multimodal self-supervised learning, enabling generalized computational reasoning supporting diagnosis, biomarker discovery, therapeutic optimization, disease monitoring, and translational oncology.[5]

3. Principles of Foundation Models for Radiopathomics

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. Rather than learning isolated predictive tasks, these models develop transferable computational knowledge applicable across diagnosis, prognosis, biomarker discovery, therapeutic optimization, disease monitoring, translational research, and clinical decision support.[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, physician documentation, patient-reported outcomes, biomedical literature, and longitudinal clinical trajectories within unified computational embedding spaces.

Graph neural networks further characterize interactions among imaging phenotypes, histopathological architecture, genes, proteins, signaling pathways, metabolites, immune populations, therapeutic targets, physiological variables, environmental exposures, and clinical outcomes, thereby enabling systems-level computational reasoning throughout precision oncology.[7]

4. Computational Architecture

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

The acquisition layer continuously integrates computed tomography, magnetic resonance imaging, positron emission tomography, ultrasound, digital pathology, genomic sequencing, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory investigations, circulating tumor DNA, physician documentation, biomedical literature, pharmacological databases, and electronic health records. Advanced preprocessing pipelines normalize imaging studies, harmonize molecular datasets, encode biomedical narratives using natural language processing, synchronize temporal

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patient information, and continuously incorporate emerging scientific evidence.

Foundation AI models subsequently generate generalized multimodal embeddings representing imaging phenotypes, tissue architecture, molecular biology, physiological function, environmental exposures, and longitudinal clinical trajectories while enabling downstream computational reasoning supporting precision oncology.[9]

5. Radiomics Intelligence

Radiomics has transformed precision oncology by enabling quantitative extraction of imaging biomarkers from computed tomography, magnetic resonance imaging, positron emission tomography, ultrasound, mammography, and hybrid imaging modalities. Foundation AI models automatically identify subtle imaging characteristics associated with tumor heterogeneity, angiogenesis, immune infiltration, metabolic activity, therapeutic responsiveness, recurrence, and survival.[10]

Multimodal transformer architectures integrate imaging-derived radiomic features with molecular biology, histopathology, laboratory biomarkers, and longitudinal clinical outcomes to generate comprehensive representations of tumor behavior. Self-supervised learning further enables discovery of previously unrecognized imaging biomarkers without requiring extensive manual annotation.

These computational advances substantially improve diagnosis, prognostic prediction, treatment planning, response assessment, and personalized oncology.[11]

6. Digital Pathology Intelligence

Digital pathology provides microscopic characterization of tumor morphology, tissue architecture, stromal composition, immune microenvironment, vascular organization, mitotic activity, necrosis, and cellular heterogeneity. Foundation AI models analyze whole-slide images using transformer architectures capable of recognizing clinically significant histopathological patterns associated with molecular alterations, therapeutic responsiveness, prognosis, and disease progression.[12]

Graph neural networks further characterize spatial cellular interactions among malignant cells, immune populations, fibroblasts, endothelial cells, extracellular matrix, and signaling pathways, thereby enabling systems-level characterization of tumor ecosystems.

Integration of pathomics with radiomics and molecular biology substantially improves diagnostic precision, biomarker discovery, prognostic modeling, and therapeutic optimization.[13]

7. Genomic Integration

Comprehensive characterization of cancer biology requires integration of genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunomics, microbiomics, single-cell sequencing, spatial transcriptomics, and spatial proteomics. Foundation AI models harmonize these diverse molecular modalities using multimodal transformers and graph neural networks capable of generating generalized molecular representations of evolving tumor biology.[14]

Artificial intelligence identifies latent biological relationships among genes, proteins, metabolites, signaling pathways, immune responses, epigenetic regulation, imaging phenotypes, histopathological architecture, and therapeutic targets while simultaneously integrating radiological information into unified computational frameworks.

These integrated molecular representations substantially improve biomarker discovery, molecular classification, therapeutic selection, precision immunotherapy, adaptive therapeutics, and translational cancer research.[15]

8. Radiogenomic and Radiopathomic Integration

One of the defining strengths of AI-enabled radiopathomics is the integration of radiological imaging with genomic and histopathological information to establish comprehensive biological representations of tumors. Foundation AI models identify associations between imaging phenotypes, microscopic tissue architecture, molecular alterations, immune signatures, laboratory biomarkers, and therapeutic response using multimodal transformer architectures and graph neural networks.[16]

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These integrated computational frameworks enable prediction of molecular biomarkers from imaging, inference of genomic alterations from histopathological architecture, identification of spatial tumor heterogeneity, and comprehensive characterization of evolving tumor ecosystems. Such capabilities substantially improve non-invasive biomarker discovery, individualized treatment planning, and translational precision oncology.

Radiogenomic integration therefore represents one of the most promising applications of multimodal artificial intelligence in modern cancer medicine.[17]

9. Intelligent Multimodal Radiopathomic Intelligence

One of the greatest strengths of foundation AI models is their ability to unify radiology, pathology, genomics, laboratory biomarkers, biomedical literature, pharmacological knowledge, electronic health records, digital biomarkers, patient-reported outcomes, and longitudinal clinical trajectories into comprehensive patient-specific computational representations. Rather than analyzing individual biomedical modalities independently, these models generate holistic representations of evolving cancer biology capable of supporting diagnosis, biomarker discovery, molecular characterization, therapeutic optimization, disease monitoring, recurrence prediction, survival estimation, multidisciplinary communication, and precision clinical decision-making. These generalized computational representations establish the foundation for radiopathomics, digital twins, intelligent clinical decision support, adaptive therapeutics, and continuously personalized precision oncology throughout the cancer care continuum.[18][19][20]

10. Digital Twins and Radiopathomic Patient Modeling

Digital twin technology represents one of the most transformative applications of AI-enabled precision radiopathomics 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 rely on isolated datasets, radiopathomic digital twins continuously update their computational representations as new multimodal biomedical information becomes available. Integration of imaging phenotypes, histopathological architecture, molecular biology, physiological monitoring, and predictive simulation enables virtual patients to evaluate multiple therapeutic strategies before implementation, optimize treatment sequencing, anticipate mechanisms of therapeutic resistance, personalize supportive care, and estimate long-term clinical outcomes according to evolving patient biology.

By integrating radiology, pathology, genomics, and predictive simulation, digital twins bridge multimodal biological understanding with individualized precision oncology.

11. Intelligent Clinical Decision Support

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

Interactive clinical dashboards generate individualized diagnostic summaries, radiomic analyses, pathomic interpretations, molecular biomarker profiles, radiogenomic correlations, digital twin simulations, therapeutic recommendations, toxicity estimates, recurrence

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probabilities, disease progression forecasts, survival predictions, 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 translational researchers.

These intelligent systems improve workflow efficiency, strengthen multidisciplinary communication, reduce fragmentation of biomedical information, and promote evidence-based personalized cancer management throughout the cancer care continuum.

12. Continuous Learning and Adaptive Radiopathomics

A defining characteristic of AI-enabled radiopathomics is the ability to continuously evolve as new biomedical information becomes available. 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, radiogenomic analysis, disease monitoring, toxicity prediction, and supportive care through iterative evaluation of longitudinal patient outcomes. Foundation AI models further integrate clinician feedback and multidisciplinary tumor board recommendations into continuous model refinement.

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

13. Federated Radiopathomic Intelligence Networks

Development of highly generalizable radiopathomic foundation 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 multimodal radiopathomic 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 investigations, liquid biopsy, electronic health records, biomedical literature, 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 radiopathomic 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. Explainability, Validation, and Ethical Governance

Successful implementation of AI-enabled precision radiopathomics requires transparent, interpretable, reproducible, and rigorously validated computational systems capable of supporting clinician confidence, patient trust, and regulatory approval. Explainable artificial intelligence (XAI) enables clinicians to understand multimodal computational reasoning through radiomic attention visualization, pathology heat maps, SHAP (Shapley Additive Explanations), integrated gradients, feature attribution analysis, uncertainty estimation, confidence calibration, multimodal attention

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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, 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 radiopathomic intelligence into routine oncology practice.

15. Future Perspectives

Future radiopathomic 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, single-cell sequencing, liquid biopsy, quantum computing, cloud-native healthcare infrastructure, biomedical knowledge graphs, retrieval-augmented generation, explainable reasoning systems, and autonomous clinical intelligence 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 coordinating molecular interpretation, adaptive therapeutics, biomarker discovery, personalized treatment planning, survivorship management, multidisciplinary communication, and continuous evidence synthesis.

Such intelligent radiopathomic ecosystems are expected to transform oncology from fragmented biomedical analysis toward predictive, adaptive, continuously learning, and precision-guided cancer medicine.

16. Discussion

AI-enabled precision radiopathomics represents one of the most significant paradigm shifts in computational oncology by integrating radiology, pathology, genomics, laboratory biomarkers, biomedical literature, pharmacological knowledge, digital biomarkers, digital twins, and foundation AI models into unified computational ecosystems capable of supporting comprehensive personalized cancer care. Unlike conventional analytical approaches that evaluate biomedical modalities independently, radiopathomic intelligence continuously synthesizes heterogeneous imaging, pathological, molecular, physiological, pharmacological, and clinical information into generalized biological representations supporting systems-level reasoning and precision medicine.[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 radiopathomic foundation models to redefine future oncology. Nevertheless, successful implementation requires continued advances in multimodal data harmonization, explainable artificial intelligence, interoperability, computational infrastructure, cybersecurity, regulatory science, ethical governance, clinician education, and sustained multidisciplinary collaboration.

As biomedical knowledge and healthcare data continue to expand exponentially, AI-enabled precision radiopathomics is expected to become one of the foundational computational infrastructures supporting precision oncology worldwide.

17. Conclusion

AI-enabled precision radiopathomics is transforming personalized cancer care by integrating radiological imaging, digital pathology, genomics, laboratory biomarkers,

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biomedical literature, electronic health records, digital biomarkers, digital twins, and foundation AI models into unified computational ecosystems capable of supporting biomarker discovery, molecular characterization, prognostic prediction, therapeutic optimization, adaptive disease monitoring, and precision 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, digital twins, agentic AI, retrieval-augmented generation, and generative artificial intelligence are expected to further strengthen radiopathomic intelligence, enabling increasingly accurate molecular characterization, predictive clinical reasoning, adaptive therapeutics, continuous disease surveillance, and personalized oncology.[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 AI-enabled precision radiopathomics. These innovations have the potential to improve patient outcomes, enhance healthcare efficiency, reduce disparities in cancer care, accelerate translational research, facilitate precision therapeutics, and establish a new era of intelligent, adaptive, and continuously learning precision oncology worldwide.[30]

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