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Next-Generation Radiomics: Foundation AI Models for High-Dimensional Imaging Biomarker Discovery

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ABSTRACT:
Radiomics has emerged as a transformative discipline in precision oncology by enabling the extraction of high-dimensional quantitative features from medical imaging that reflect tumor phenotype, biological heterogeneity, and therapeutic response. Traditional radiomics relies on handcrafted imaging features and conventional machine learning algorithms, which often exhibit limited reproducibility and generalizability across imaging platforms and patient populations. Recent advances in foundation artificial intelligence (AI) models have fundamentally redefined radiomics through self-supervised learning, transformer architectures, multimodal representation learning, graph neural networks, and generative AI capable of learning generalized imaging representations from massive collections of radiological data. Integration of radiological imaging with digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, electronic health records, and longitudinal clinical outcomes has expanded radiomics into comprehensive multimodal computational ecosystems supporting precision diagnosis, biomarker discovery, therapeutic prediction, adaptive treatment planning, digital twins, and intelligent clinical decision support. Emerging technologies including large language models, retrieval-augmented generation, federated learning, reinforcement learning, explainable artificial intelligence, and agentic AI further enhance the translational potential of imaging-based computational oncology. Despite remarkable advances, significant challenges remain regarding imaging standardization, data harmonization, computational scalability, interpretability, interoperability, regulatory validation, and ethical implementation. This review provides a comprehensive overview of next-generation radiomics, emphasizing foundation AI models for high-dimensional imaging biomarker discovery, clinical applications, implementation challenges, and future perspectives for precision oncology.[1]

Keyword: Radiomics, Foundation models, Artificial intelligence, Precision oncology, Imaging biomarkers, Radiogenomics, Computational imaging, Medical imaging, Personalized medicine, Clinical decision support.

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1.Introduction

Medical imaging plays a central role in oncology by supporting cancer detection, diagnosis, staging, treatment planning, therapeutic monitoring, and long-term surveillance. Conventional radiological interpretation primarily relies on qualitative visual assessment by expert radiologists, which, although highly valuable, captures only a fraction of the biological information contained within modern medical images.[2]

Radiomics has emerged as an innovative computational approach that converts standard medical imaging into quantitative high-dimensional data describing tumor morphology, texture, intensity, shape, vascularity, metabolism, spatial heterogeneity, and temporal evolution. These imaging biomarkers provide non-invasive insights into tumor biology that complement molecular diagnostics and histopathological evaluation.[3]

Traditional radiomics has largely depended upon handcrafted feature engineering followed by conventional machine learning algorithms. However, variability in image acquisition, segmentation methods, feature extraction protocols, and statistical modeling has limited reproducibility and widespread clinical implementation.

Foundation artificial intelligence models have fundamentally transformed radiomics by enabling automated representation learning from massive imaging datasets while integrating radiological information with pathology, multi-omics, laboratory biomarkers, and longitudinal clinical intelligence. These advances are redefining computational imaging and precision oncology.[4]

2.Evolution of Radiomics

The earliest generation of radiomics focused on extraction of predefined quantitative imaging features describing tumor shape, first-order intensity statistics, texture patterns, and wavelet transformations. These handcrafted descriptors demonstrated considerable potential for predicting diagnosis, prognosis, and therapeutic response but frequently lacked robustness across institutions and imaging platforms.[5]

Subsequent advances in deep learning enabled automatic extraction of hierarchical imaging features directly from raw medical images without requiring manual engineering. Convolutional neural networks substantially improved lesion detection, segmentation, classification, and outcome prediction across numerous malignancies.

Recent development of transformer architectures and foundation AI models has further expanded radiomics through generalized representation learning capable of transferring knowledge across imaging modalities, cancer types, and clinical applications while reducing dependence on extensive manual annotation.[6]

Today, next-generation radiomics integrates computational imaging, systems biology, multimodal learning, and precision medicine into unified intelligent oncology ecosystems supporting individualized cancer management.[7]

3.Foundation AI Models in Radiomics

Foundation AI models differ fundamentally from conventional radiomics algorithms because they are pretrained on extremely large collections of radiological images before adaptation to specialized clinical applications. Rather than learning isolated prediction tasks, these models acquire generalized imaging representations applicable across diagnosis, biomarker discovery, prognostic assessment, therapeutic prediction, and clinical decision support.[8]

Self-supervised learning enables discovery of latent imaging features without extensive manual annotation, whereas transformer architectures efficiently model long-range spatial relationships within high-resolution medical images. Cross-modal representation learning further integrates radiological imaging with digital pathology, genomics, laboratory biomarkers, and electronic health records into unified computational embeddings.

Graph neural networks strengthen biological reasoning by modeling interactions among imaging phenotypes, molecular pathways, tissue architecture, therapeutic targets, and clinical outcomes, thereby enhancing the biological interpretability of imaging biomarkers.[9]

4.Computational Architecture

Modern next-generation radiomics platforms consist of interconnected computational layers responsible for image acquisition, preprocessing, representation learning, multimodal integration, predictive analytics, adaptive model refinement, and intelligent clinical decision support.[10]

The acquisition layer incorporates computed tomography, magnetic resonance imaging, positron emission tomography, ultrasound, hybrid imaging modalities, laboratory biomarkers, pathology reports, genomic sequencing, and longitudinal clinical records. Advanced preprocessing pipelines perform image normalization, artifact correction, registration, segmentation, and harmonization across imaging platforms.

Transformer-based foundation models generate generalized imaging embeddings representing anatomical structures, tissue heterogeneity, vascular patterns, metabolic activity, and tumor morphology. Multimodal fusion layers subsequently integrate these imaging features with molecular biology and clinical information into comprehensive patient-specific computational representations supporting precision oncology.[11]

5.High-Dimensional Imaging Biomarker Discovery

One of the greatest strengths of foundation AI models lies in their ability to discover high-dimensional imaging biomarkers directly from raw medical images without requiring predefined handcrafted features. Artificial intelligence automatically identifies subtle imaging patterns associated with tumor biology, immune infiltration, angiogenesis, hypoxia, necrosis, fibrosis, vascular remodeling, metabolic adaptation, and therapeutic responsiveness.[12]

These computational biomarkers frequently capture latent biological information that remains invisible during routine radiological interpretation. Deep representation learning substantially improves robustness while enabling transferability across multiple imaging modalities and cancer types.

High-dimensional imaging biomarkers therefore provide increasingly comprehensive characterization of tumor heterogeneity while supporting individualized diagnosis, prognostic prediction, biomarker discovery, and treatment planning.[13]

6.Radiogenomics and Multimodal Integration

Radiogenomics represents one of the most important applications of next-generation radiomics because it establishes relationships between imaging phenotypes and underlying molecular biology. Foundation AI models integrate radiological imaging with genomics, transcriptomics, proteomics, metabolomics, epigenomics, spatial biology, laboratory biomarkers, and digital pathology into unified computational frameworks.[14]

Multimodal transformers, graph neural networks, and biological knowledge graphs identify complex associations among imaging features, genomic mutations, signaling pathways, immune responses, protein expression, and therapeutic targets that remain difficult to detect using isolated analytical methods.

These integrated computational representations substantially improve molecular subtype classification, biomarker discovery, therapeutic response prediction, precision medicine, and systems oncology research.[15]

7.Artificial Intelligence for Tumor Characterization

Foundation AI models enable comprehensive characterization of tumors by integrating anatomical morphology, functional imaging, metabolic activity, vascular architecture, spatial heterogeneity, and temporal evolution into unified computational representations. Unlike conventional imaging assessment based primarily on lesion size, AI-derived imaging biomarkers capture multiple dimensions of tumor biology simultaneously.[16]

These intelligent computational systems automatically quantify tumor burden, invasion patterns, angiogenesis, hypoxia, necrosis, fibrosis, metastatic dissemination, and treatment-induced biological alterations while supporting diagnosis, staging, therapeutic planning, and disease monitoring.

Such multidimensional characterization substantially strengthens precision oncology by providing comprehensive, non-invasive assessment of evolving tumor biology across the entire patient journey.[17]

8.Predictive Radiomics in Precision Oncology

Predictive radiomics has become increasingly important for individualized therapeutic decision-making because imaging biomarkers provide non-invasive assessment of biological characteristics associated with treatment response. Foundation AI models integrate radiological imaging with pathology, molecular diagnostics, laboratory biomarkers, medication history, wearable physiological monitoring, and longitudinal clinical outcomes into adaptive predictive frameworks.[18]

Artificial intelligence estimates responsiveness to chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, surgery, and multimodal treatment combinations while simultaneously predicting recurrence probability, progression-free survival, overall survival, treatment-related toxicity, and mechanisms of therapeutic resistance.

These adaptive predictive imaging systems substantially improve personalized therapeutic planning while reducing unnecessary treatment-related morbidity and supporting evidence-based precision medicine.[19]

9.Imaging Biomarkers for Longitudinal Disease Monitoring

Medical imaging provides continuous, non-invasive assessment of tumor evolution throughout diagnosis, treatment, follow-up, and survivorship. Foundation AI models analyze serial imaging examinations to characterize temporal changes in tumor morphology, vascularity, metabolism, tissue heterogeneity, and treatment response. These longitudinal imaging biomarkers facilitate early detection of recurrence, therapeutic resistance, minimal residual disease, and metastatic progression while supporting adaptive clinical decision-making throughout the cancer care continuum.[20]

10.Foundation AI Models for Treatment Response Prediction

One of the most clinically significant applications of next-generation radiomics is the prediction of therapeutic response using high-dimensional imaging biomarkers derived from foundation AI models. Unlike conventional radiological assessment, which primarily evaluates anatomical changes after treatment, foundation models analyze complex imaging phenotypes that reflect underlying biological processes before macroscopic alterations become clinically apparent.[21]

Artificial intelligence integrates computed tomography, magnetic resonance imaging, positron emission tomography, digital pathology, multi-omics, laboratory biomarkers, medication history, and longitudinal clinical outcomes into unified computational representations capable of predicting responsiveness to chemotherapy, targeted therapy, endocrine therapy, immunotherapy, radiation therapy, and multimodal treatment strategies. These predictive imaging models enable earlier therapeutic optimization while minimizing ineffective treatments and unnecessary toxicity.

11.Digital Twins and Imaging-Based Virtual Oncology

Digital twin technology has emerged as one of the most innovative applications of next-generation radiomics. AI-powered digital twins integrate serial imaging studies, digital pathology, genomics, transcriptomics, proteomics, metabolomics, laboratory biomarkers, liquid biopsy, wearable physiological monitoring, treatment history, and longitudinal clinical information into continuously evolving virtual patient models.[22]

Foundation AI models synchronize these virtual representations with biological patients, allowing simulation of tumor growth, metastatic dissemination, therapeutic response, treatment-related toxicity, recurrence, and survival under multiple therapeutic scenarios before actual clinical intervention.

Imaging-driven digital twins support individualized therapeutic optimization while enabling clinicians to evaluate alternative treatment strategies using patient-specific computational simulations.

12.Continuous Learning Radiomics

Radiomics is increasingly evolving from static image analysis toward continuously learning computational ecosystems capable of adapting as new biomedical information becomes available. Foundation AI models continuously integrate serial radiological examinations, computational pathology, circulating tumor DNA, laboratory biomarkers, wearable physiological monitoring, electronic health records, and real-world clinical outcomes into adaptive predictive frameworks.[23]

Continuous learning enables imaging biomarkers to evolve alongside tumor biology while maintaining alignment with emerging scientific evidence and changing patterns of clinical practice. Reinforcement learning further optimizes therapeutic recommendations by incorporating feedback from previous treatment outcomes.

These adaptive radiomics platforms represent a major advancement toward real-time precision oncology capable of supporting dynamic therapeutic decision-making.

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13. Intelligent Clinical Decision Support

Foundation AI models provide the computational foundation for intelligent imaging-based clinical decision-support systems. These platforms integrate radiological imaging, computational pathology, molecular diagnostics, laboratory investigations, medication history, wearable technologies, physician documentation, and evidence-based treatment guidelines into comprehensive patient-centered computational environments.[24]

Interactive clinical dashboards generate automated lesion characterization, imaging biomarker analyses, molecular interpretations, prognostic estimates, therapeutic recommendations, toxicity predictions, recurrence probabilities, and survival forecasts while facilitating multidisciplinary collaboration among radiologists, oncologists, pathologists, surgeons, molecular biologists, radiation oncologists, and computational scientists.

Such intelligent systems improve workflow efficiency, reduce diagnostic variability, and strengthen evidence-based clinical decision-making throughout oncology practice.

14. Explainability, Validation, and Regulatory Considerations

Successful implementation of next-generation radiomics requires transparent, interpretable, and scientifically validated artificial intelligence systems. Explainable artificial intelligence (XAI) enables clinicians to understand computational reasoning through attention heatmaps, saliency visualization, SHAP (Shapley Additive Explanations), feature attribution analysis, uncertainty estimation, and counterfactual explanations identifying imaging features responsible for predictive outputs.[25]

Clinical translation also requires standardized imaging acquisition protocols, harmonized preprocessing pipelines, interoperable computational infrastructure, prospective multicenter validation, continuous monitoring for algorithmic bias, external benchmarking, cybersecurity safeguards, and compliance with evolving international regulatory frameworks governing AI-enabled medical technologies.

Responsible implementation further depends upon ethical governance emphasizing patient privacy, transparency, accountability, equitable access, informed consent, and post-deployment monitoring.

15. Future Perspectives

Future radiomics ecosystems will increasingly integrate multimodal foundation models, large language models, agentic artificial intelligence, graph neural networks, federated learning, reinforcement learning, digital twins, spatial multi-omics, quantum computing, cloud-native healthcare infrastructure, and Internet of Medical Things (IoMT) technologies into unified computational imaging platforms.[26]

These next-generation systems will continuously integrate radiological imaging, digital pathology, molecular biology, laboratory medicine, wearable physiological monitoring, environmental exposures, electronic health records, and real-world clinical outcomes while autonomously coordinating diagnostic workflows, generating imaging reports, optimizing therapeutic recommendations, and supporting continuous biomedical evidence synthesis.

Such intelligent imaging ecosystems are expected to transform radiomics from image interpretation toward comprehensive computational oncology capable of continuously adapting throughout the patient journey.

16. Discussion

Next-generation radiomics represents a fundamental paradigm shift in computational imaging by replacing handcrafted feature engineering with generalized representation learning enabled by foundation AI models. These intelligent systems integrate imaging biomarkers with molecular biology, digital pathology, laboratory investigations, and longitudinal clinical intelligence into unified computational frameworks capable of supporting precision diagnosis, biomarker discovery, prognostic assessment, therapeutic optimization, and adaptive disease monitoring.[27]

Applications including radiogenomics, computational pathology integration, digital twins, continuous learning systems, intelligent clinical decision support, and multimodal precision oncology demonstrate the extraordinary potential of foundation AI models to redefine imaging-based cancer care. Nevertheless,

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successful implementation requires continued advances in multimodal data harmonization, explainable artificial intelligence, interoperability, computational infrastructure, regulatory science, cybersecurity, and multidisciplinary collaboration.

As increasingly comprehensive biomedical datasets become available, next-generation radiomics will become an essential pillar of intelligent precision oncology.

17.Conclusion

Foundation AI models are redefining radiomics by transforming medical imaging into a comprehensive source of high-dimensional biological intelligence capable of supporting precision oncology throughout the cancer care continuum. Integration of radiological imaging with digital pathology, multi-omics, laboratory biomarkers, wearable technologies, and longitudinal clinical information enables increasingly accurate diagnosis, biomarker discovery, molecular characterization, therapeutic response prediction, adaptive treatment planning, and evidence-based clinical decision-making.[28]

Advances in transformer architectures, multimodal learning, graph neural networks, self-supervised learning, digital twins, federated learning, reinforcement learning, large language models, agentic AI, and generative artificial intelligence are expected to further strengthen computational imaging while accelerating translation of high-dimensional imaging biomarkers into routine clinical practice.[29]

Although important scientific, technical, ethical, regulatory, and implementation challenges remain, continued collaboration among radiologists, oncologists, pathologists, molecular biologists, biomedical engineers, computer scientists, healthcare organizations, imaging scientists, and regulatory agencies will accelerate responsible implementation of next-generation radiomics. These innovations have the potential to improve patient outcomes, enhance diagnostic precision, optimize therapeutic selection, reduce healthcare disparities, and establish a new era of intelligent imaging-driven precision cancer medicine worldwide.[30]

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