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Mini-review

Deep Learning of radiology-genomics integration for computational oncology: A mini review

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ABSTRACT

In the field of computational oncology, patient status is often assessed using radiology-genomics, which includes two key technologies and data, such as radiology and genomics. Recent advances in deep learning have facilitated the integration of radiology-genomics data, and even new omics data, significantly improving the robustness and accuracy of clinical predictions. These factors are driving artificial intelligence (AI) closer to practical clinical applications. In particular, deep learning models are crucial in identifying new radiology-genomics biomarkers and therapeutic targets, supported by explainable AI (xAI) methods. This review focuses on recent developments in deep learning for radiology-genomics integration, highlights current challenges, and outlines some research directions for multimodal integration and biomarker discovery of radiology-genomics or radiology-omics that are urgently needed in computational oncology.

1. Introduction

Cancer is one of the most complex and challenging diseases, the second leading cause of death and a significant global public health problem. Its progression involves a series of complex changes at both microscopic and macroscopic levels, but the underlying functional interactions and mechanisms are not yet fully understood [1,2]. This complexity of tumorigenesis is reflected in the diversity of data collected during a patient's diagnosis and treatment. These data span multiple modalities, from radiology, histology, molecular profiling to family history, each providing unique insights into the patient's condition [3,4]. The complex and heterogeneous nature of cancer requires an equally comprehensive approach to diagnosis, treatment and management, which recognize the critical role of multimodal data in understanding this disease [5].

Among these various modalities, radiology and genomics stand out as cornerstones of modern oncology, providing deep insights into the nature of cancer at both macroscopic and microscopic levels. Radiology is a crucial tool in clinical detection and decision-making in cancer treatment, with radiological imaging serving as a non-invasive and cost-effective method that takes into account functional characteristics and heterogeneity [6]. Tissue-scale imaging allows radiology to examine not only the regions affected by the disease, but also the surrounding structures, such as the peritumoral region. In particular, computed tomography (CT), magnetic resonance imaging (MRI), and radiographs can detect premalignant lesions based on the three-dimensional images they produce. These images are used in various models for cancer diagnosis, prognosis and treatment response prediction.

Compared to imaging in radiology, genomic data analysis deals with molecular and cellular activities at the microscopic level. Advances in high-throughput sequencing technologies have enabled the establishment of large-scale cancer research platforms, including projections of paired multi-omics cancer datasets from the Cancer Genome Atlas (TCGA) [7] and the International Cancer Genome Consortium (ICGC) [8] across different cancer types. These datasets provide comprehensive information for understanding the pathogenesis and progression of cancers, but also present challenges for integrated analysis of multi-omics in precision oncology studies [4]. Notably, these datasets

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focus primarily on genomic analysis of tumor tissue samples, which focuses on somatic mutations occurring in tumor cells by pathologists and molecular biologists. This is different from germline mutations, which are inherited present in every cell of the body and typically analyzed by geneticists. Interestingly, several studies have shown that medical images can help infer visual phenotypes that serve as proxies or biomarkers for molecular phenotypes (e.g., epidermal growth factor receptor mutations in lung cancer) [9–12]. An emerging field called 'radiology-genomics', aims to link imaging features to underlying molecular properties [13], which typically focuses on genomics data but could also include transcriptomics, metabolomics, deep pathomics and other emerging omics data.

Recent advances in deep learning methods have demonstrated the significant potential of representation learning and latent space integration, which improve the predictive performance of many clinically relevant applications, including complicated and redundant tasks that are often nontrivial to human observers [14–16]. By integrating complementary information, deep learning methods can capture nonlinear relationships between radiology and genomics data sources, enabling more accurate patient predictions [5,17]. Clinical outcome can initially be accurately predicted by successful models and then elucidated by interpretation methods to guide and accelerate the discovery of new

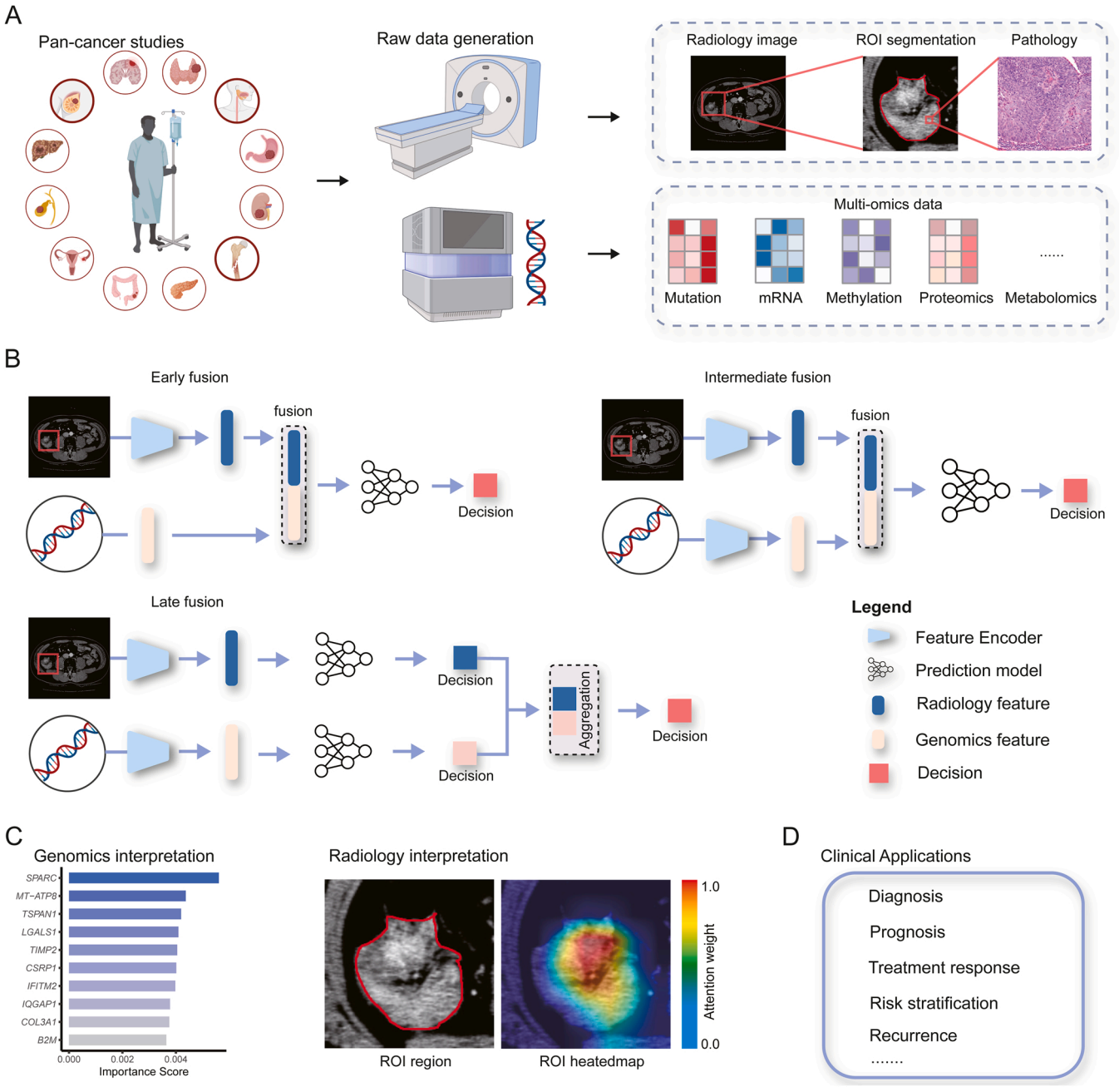

Fig. 1. Overview of deep learning in radiology-genomics for precision oncology. a. Radiology-genomics data generation in pan-cancer studies. b. The diagram of Radiology-genomics integration based on deep learning, including early, intermediate and late fusion. Early fusion combines raw data at the input level. Intermediate fusion optimizes feature representations by backpropagating prediction errors. Late fusion aggregates predictions from independently trained models. c. Interpretability and introspection of deep learning models for Radiology-genomics. On one hand, importance of genomics features can be analyzed by integrated gradient (IG) in patients level. On the other hand, GradCAM can employ highlighting significant areas in radiology images. d. Radiology-genomics fusion for multiple clinical applications. The drawings in panel A were created with BioRender.com.

genomic and radiological biomarkers [6].

The aim of this mini-review is to delve into the intricacies of deep learning in radiology-genomics integration for computational oncology and to explore the role of radiology and genomics in improving clinical applications that also relate to the integration of radiology and new omics data (Fig. 1**A**). This study will illustrate the potential of deep learning-based precision oncology to improve the diagnosis, treatment and management of cancer and contribute to more interpretive and personalized medicine.

2. Deep learning methods applicable in radiology-genomics data analysis

Deep learning models are designed to extract nonlinear informative representations and encode high-dimensional data into a low-dimensional embedding space for subsequent tasks. Different models are specifically designed for feature extraction from different data sources, each playing a crucial role in the analysis of radiology-genomics data (Fig. 2).

(1) **Variational Autoencoders (VAEs).** Variational autoencoders (VAEs), extensions of traditional autoencoders, learn a low-dimensional representation of input data and can generate from a latent distribution (Fig. 2**A**). VAEs include the neural network component of the encoder and decoder, which is connected through a latent space regularized by the prior distribution of the normal Gaussian distribution. The encoder transforms the input data into a latent space that captures the underlying Gaussian distribution of the mean and variance. This latent representation is then sampled from this distribution. The decoder reconstructs the input data from this latent representation. The VAE loss function combines reconstruction loss with Kullback—Leibler divergence between variational distribution and prior distribution, ensuring the regularity of data generation and distribution. Their ability to model complex, high-dimensional data distributions has been instrumental in advancing the field of deep generative models and providing new insights and methods [18]. VAEs have transformed genomics and radiomics by enabling advanced pattern and biomarker recognition, significantly improving disease diagnosis and personalized medicine.

(2) **Convolutional neural networks (CNNs).** Convolutional neural networks (CNNs) are designed for modeling spatial structures such as images or DNA sequences. Its architecture includes feature extraction based on convolutional filter layers, dimensionality reduction based on pooling layers, and classification based on fully connected layers, which can leverage spatial hierarchies (Fig. 2**B**). Convolutional layers apply filters to capture local dependencies and translational invariance, making CNNs suitable for image data. Pooling layers reduce the spatial size, decrease the number of parameters and reduce the computational burden in the network. CNNs have revolutionized the field of medical imaging by enabling automatic and efficient analysis for both diagnostics [9,19,20] and prognosis prediction [21,22], highlighting their critical importance in improving health outcomes.

(3) **Vision transformers (ViTs).** Vision transformers (ViTs) utilize the transformer architecture, best known for their success in natural language processing [23,24]. Unlike CNNs, ViTs do not rely on the inductive biases of convolutional layers and instead use self-attention mechanisms to process images as sequences of patches. ViTs divide an image into patches of fixed-size and process these patches sequentially, similar to words in a sentence (Fig. 2**C**). In radiology, ViTs have shown exceptional promise, particularly in analyzing CT and MRI scans. The ability of these methods to detect complicated patterns and anomalies in medical images has remarkable implications for diagnosis and treatment planning [25,26] and improves the accuracy and efficiency of radiological examinations.

(4) **Graph neural networks (GNNs).** Graph neural networks (GNNs) excel particularly in areas where data is inherently structured as graphs [27,28]. This is particularly evident in specialty areas such as radiology and genomics, where GNN offers unprecedented analytical capabilities. GNNs process graph-structured data, where nodes represent entities and edges represent relationships (Fig. 2**D**). They capture complex dependencies and relationships within this data using layers that iteratively update the representation of each node based on its neighbors [29]. This approach enables GNNs to effectively learn complex relationship structures. In radiology, GNNs have been instrumental in analyzing complex image data and identifying patterns and anomalies in interconnected pixel images. Similarly, in genomics, GNNs

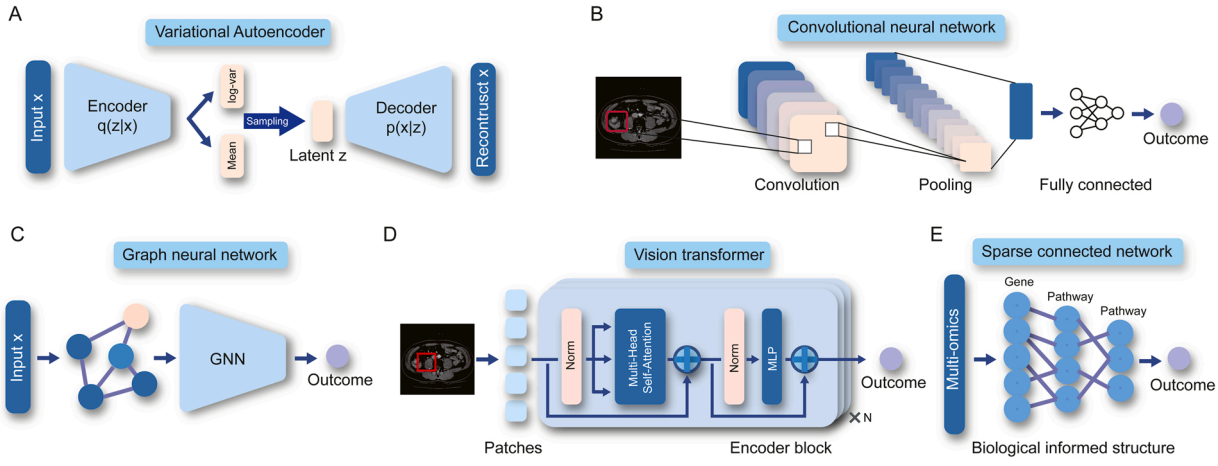

Fig. 2. Scheme overview of deep learning models. a. Variational autoencoders (VAEs) learn a low-dimensional representation of input data and can generate from a latent distribution. b. Convolutional neural networks (CNNs) can extract image features based on convolutional filter layers, dimensionality reduction based on pooling layers, and classification based on fully connected layers, ultimately allowing spatial hierarchies to be exploited. c. Vision transformers (ViTs) utilize the transformer architecture and self-attention mechanisms, that divide an input image into patches of fixed-size and process these patches sequentially, similar to words in a sentence. d. Graph neural networks (GNNs) can process graph-structured data, where nodes represent entities and edges represent relationships, and therefore excel particularly in domains where data is inherently structured as graphs. e. Sparse connected networks (SCNs) have selective and limited connections between hidden layer nodes that correspond to biological processes or pathways that are different from traditional densely connected networks.

decipher complex networks of genetic interactions [29–31] and help understand genetic diseases [32,33].

(5) **Sparse connected networks (SCNs).** Sparse connected networks have proven to be a significant advance in computational biology, particularly in the integration of genomic data (Fig. 2**E**). Unlike traditional densely connected networks, SCNs have selective and limited connections between hidden layer nodes that correspond to biological processes or pathways [34,35]. This design improves the biological interpretability of the "black-box" model and better adapts to the actual structure of biological systems. SCNs improve model efficiency and reduce overfitting, which is critical in medical fields where data is often scarce and complex. For instance, P-NET [36], a biologically informed deep neural network, was developed to detect prostate cancer. In addition, PAUSE [37], which stands for Principled Feature Attribution for Unsupervised Gene Expression Analysis, is another example of how these networks can be used for insightful gene expression analysis.

In addition, a feature summary of the various deep learning methods mentioned above in radiology-genomics data analysis is presented in Table 1, showing their potential pros and cons in specific application scenarios.

3. Deep learning framework for radiology-genomics fusion

By deploying advanced multimodal fusion technologies, deep learning has proven effective in single-modality analysis of radiology and genomics profiles. The integration of radiology and genomics aims to uncover connections between microscopic molecular and macroscopic information of organisms, thereby enabling a more comprehensive representation of disease mechanisms. Deep learning-driven fusion strategies can be classified into early, intermediate and late fusion frameworks, each providing unique computational advantages and task considerations (Fig. 1**B and** Table 2).

(1) **Early fusion framework.** Early fusion integrates information from multiple data sources at the input stage and then processes it into a single model. Techniques such as concatenation, elementwise summation, multiplication or bilinear pooling (Kronecker product) produce a common representation at the input layer, which approaches a streamlined model design by using a single model for feature extraction. Early fusion allows for flexible data combination, but potentially overlooks inherent differences in data format, distribution, and spatial characteristics between modalities. In scenarios where the modalities have significant differences in distribution and data space, early fusion methods may not be ideal, resulting in suboptimal fusion performance. Despite this limitation, early fusion methods have shown promise in clinical use and have been successfully used in various oncology applications, such as fusion of computed tomography (CT) and/or MRI data with gene expression data for cancer detection [38], treatment planning [39,40] or survival prediction [41]. Several studies have examined the correlated changes in gene expression and integrated them into radiological images for cancer detection in lung cancer [42], classification [43], survival [44] and prediction of treatment response [45].

(2) **Intermediate fusion framework.** In intermediate fusion, multimodal features are combined at an intermediate stage of the model architecture, typically after the initial feature extraction but before the final decision level, such as concatenation, elementwise operations or more sophisticated attention mechanisms [46–48]. These methods allow preservation of modality-specific information prior to integration, eliminating some of the limitations associated with early fusion and providing a balance between the simplicity of early fusion and preservation of the modality-specific features of late fusion. By considering both shared and modality-specific representations, these methods aim to achieve more effective integration in scenarios where early fusion may be difficult due to significant distribution differences between modalities. Examples of intermediate fusions in oncology include the integration of different radiological imaging modalities, such as detection of lung cancer by fusion of PET and CT scans [49–51], classification of prostate cancer by fusion of MRI and ultrasound images [52] and glioma segmentation by combination of multimodal MRI scans [53,54]. Genomic data along with mammography images have also been used to improve survival prediction [55].

(3) **Late fusion framework.** Late fusion, or so-called decision-level fusion, is developed to train modality-specific models and predict the final outcome by aggregating the predictions of all individual models, including averaging, majority voting, Bayes-based rules, or learned models such as MLP. Late fusion provides different model architecture for each modality, avoiding modality correlation concerns or data synchronization limitations. It is suitable for complex systems with multiple data sources or significant

Table 1
Feature summary of deep learning methods in radiology-genomics data analysis.

Method	VAEs	CNNs	ViTs	GNNs	SCNs
Flexible encoding and decoding	√				√
Unsupervised learning	√				
Excellent for image data		√			
Capture of local dependencies		√			
Self-attention mechanism			√		
Detection of complex pattern			√	√	
Capture of intricate dependencies in graph-structured data				√	
Reduction of over-fitting					√
Biological interpretation				√	√

Table 2
Pan-cancer radiology-genomics studies (part 1).

Cancer type	Study ID	Study Objective	Integration method	Reference list
Gliomas	G1	Molecular subtype	-	Buda, M. et al. [108]
	G2	Molecular subtype	-	Li, Y. et al.[109]
Breast cancer	B1	Oncotype Dx RS	-	Ha, R. et al. [110]
	B2	Predicting molecular subtypes	-	Ha, R. et al. [111]
	B3	Molecular subtypes	-	Zhang, Y. et al. [112]
Lung cancer	L1	Gene mutation prediction	-	Hosny, A. et al. [113]
	L2	Gene mutation prediction	-	Song, Y.[42]
	L3	Molecular subtype	-	Yamamoto, S. et al.[114]
Medulloblastoma	M1	Molecular subtypes	-	Dasgupta, A. et al.[115]
Renal Cancer	R1	Prognosis Prediction	Early fusion	Schulz, S. et al. [44]
Colorectal cancer	C1	metastasis prediction	Early fusion	Zhao, J. et al. [43]
Lung cancer	L4	Recurrence prediction	Intermediate fusion	Jia, L. et al. [116]
Brain cancer	B4	Prognosis prediction	Intermediate fusion	Cui, C. et al. [117]
Lung cancer	L5	Prognosis prediction	Early fusion	Chen, W. et al. [118]

data heterogeneity. When data is missing or incomplete, late fusion can still make predictions by training each modality model separately and aggregating predictions even if a modality is not available. In oncology, There are many late fusion applications involving the integration of imaging data with genomic data in the fusion of CT and genomic profiles for lung cancer diagnosis [56], prostate cancer survival prediction [57,58] and chemotherapy response prediction [45], could be used.

4. Task-aware deep learning advances in radiology-genomics for precision oncology

Over the last decade, radiology-genomics has emerged as a synergistic field that combines radiology and genomics and aims to address the limitations of current diagnostic methods. This interdisciplinary approach facilitates the development of noninvasive diagnostic and prognostic tools by combining the quantitative imaging characteristics of tumor phenotypes with genomic data. Such integration is promising for the identification of therapeutic biomarkers, particularly in oncology, and for the further development of personalized medicine. Radiology-genomics, enhanced by the molecular characterization of various types of cancer and the application of texture analysis and deep learning techniques contributes significantly to the advancement of cancer diagnostics towards individualized treatment paradigms.

(1) **Molecular status determination for cancer diagnosis.** Accurately identifying the molecular phenotype of tumors is crucial for cancer diagnosis in the era of precision medicine (e.g. cases shown in Table 2 and Table 3). This task is complicated by the heterogeneity of malignant tumors, which often results in small biopsy samples being insufficient to capture the full spectrum of tumor gene mutations. Radiology-genomics offers a promising solution by studying the relationship between imaging features and molecular markers of tumors. The aim of this approach is to provide a noninvasive means of predicting gene mutations from imaging data, overcoming the limitations of traditional, invasive biopsy methods, which are costly, time-consuming, and not universally accessible. Integrating imaging phenotypes with molecular phenotypes using Radiology-genomics not only facilitates precision medicine but also paves the way for more effective cancer diagnosis and treatment strategies [17,59]. Initial research has shown a correlation between radiological imaging patterns and biological molecular conditions, suggesting that phenotypes detected from medical images may serve as surrogates or biomarkers for molecular phenotypes, such as epidermal growth factor receptor (EGFR) mutations in lung cancer highlighting the ability of radiology-genomics to substantially increase the precision of cancer detection [60]. These findings suggest that integrated radiology-genomics approaches could be used to identify eligible and noneligible patients for targeted therapies, potentially streamlining clinical decision-making processes. In particular, in many scenario of early cancer diagnosis, it is difficult to obtain tumor tissue samples. Therefore, blood samples could be adopted and such predictive approaches can help physicians make informed decisions.

(2) **Personalized care response prediction for cancer treatment.** Recent studies have significantly advanced the field of imaging genomics, and demonstrated that the imaging properties of tumor tissue can accurately predict response to various therapies, including chemotherapy, radiotherapy, targeted therapy, and immunotherapy. Chemotherapy and radiotherapy largely target cancer cells, while targeted therapy and immunotherapy attack specific molecular signaling pathways and strengthen the immune system. This advance facilitates the personalization of treatment strategies, and allows clinicians to predict an individual patient's response to specific therapeutic interventions, thereby optimizing treatment effectiveness while minimizing toxicity [61,62]. Such a tailored treatment approach significantly reduces unnecessary medical interventions, reduces the risk of side effects and increases the likelihood of therapeutic success [63].

(3) **Prognosis and risk stratification for cancer patients.** The integration of radiology and genomics facilitates the development of prognostic markers by bringing together imaging, genetic and pathological data. This synthesis unveils the relationship between imaging characteristics and patient outcomes, thereby accelerating the translation of radiology-genomics into clinical practice. By adopting this personalized approach, therapeutic interventions are aligned with individual prognoses, thereby improving resource efficiency and overall health care [20,64]. Moreover, risk stratification enabled by radiology-genomics can significantly influence resource allocation and patient management [17]. This approach allows high-risk patients to be

Table 3
Pan-cancer radiology-genomics studies (part 2).

Study ID	Genomics data on tumor tissue	Imaging modality	Imaging model	Clinical Requirement *
G1	DNA methylation, gene expression, DNA copy number, and microRNA expression, as well as IDH mutation 1p/19q co-deletion measurement	MRI	Cross-validation model	PD, PA
G2	Known genomic marker status based on 2016 WHO classification	MRI	CNN	PD, PA
B1	Marker genes based on Oncotype DX	MRI	CNN	PA
B2	Immunohistochemical staining pathology data	MRI	CNN	PD,PA
B3	Hormonal receptor (HR) and HER2 receptor: (HR+/HER2 −), HER2 + and triple negative (TN)	MRI	CNN	PD,PA
L1	Tumor node metastasis stage and gene expression assays	CT	CNN	SD,PT
L2	EGFR and KRAS mutation status	CT	CNN	SD,PT
L3	ALK status and clinical-pathologic	CT	Random forest	PD,PA
M1	Marker profiling of 12 protein coding genes and 9 microRNAs using real-time reverse transcriptase polymerase chain reaction	MRI	Multivariate logistic regression analysis	PD,PA
R1	Genomic data from whole exome sequencing	CT	CNN	SP,PT
C1	RNA sequencing for paired tissues (CRC tissues and adjacent normal tissues)	CT	CNN	SD
L4	Gene Expression from RNA-seq	CT	CNN	RP,PT
B4	80 DNA features including 79 of the most expressive CNV features and one binary indication of mutation status for IDH1 gene	CT	CNN	SP,PT
L5	Gene Expression from RNA-seq	CT	CNN	SP,PT

* Clinical requirements include precise diagnosis (PD), prognosis assessment (PA), personalized treatment (PT), stage diagnosis (SD), survival prediction (SP), and recurrence prediction (RP).

prioritized and ensures they receive immediate and intensive care. In addition, it facilitates the efficient allocation of medical resources and optimizes the use of available treatments and interventions based on individual risk profiles identified through radiology-genomics analysis. Identifying high-risk patients allows prioritization of more rigorous monitoring and timely interventions to ensure they receive the necessary care promptly [65]. Conversely, low-risk individuals benefit from a less intensive treatment strategy, thereby minimizing unnecessary healthcare expenditure and mitigating the risks associated with overtreatment [66].

5. Interpretation of the deep learning model improves the integration of radiology and genomics

In radiology-genomics, deep learning models can learn abstract feature representations. However, there is concern that these models may use incorrect shortcuts for predictions instead of learning relevant clinical aspects. In another words, despite the improvement of deep learning in various tasks for clinical requirements (Table 3), there are still concerns about the clinical decision-making process of AI due to the property 'black box' of deep neural networks. Therefore, interpretability and model introspection should be crucial topics in AI for the integration of radiology and genomics (**Fig.1CD**), encompassing different phases of model development, deployment and validation.

(1) **Radiology interpretability from deep learning.** In radiology, interpretability methods are essential to understand the importance of different image regions in deep learning model predictions. Techniques such as class activation maps (CAMs), including Grad-CAM and Grad-CAM++ [67,68], are crucial for identifying the importance of individual pixels in the decision-making process involved in deep learning. These methods evaluate how changes in inputs, such as pixels in radiological images, affect the model's output. Grad-CAM, combined with guided backpropagation, determines pixel-level importance within prediction regions. By overlaying attention scores on radiology scans, key regions that contribute to outcome predictions are visualized using heatmaps. Studies using Grad-CAM have enabled slide-level interpretability in tasks such as lung cancer diagnosis and survival prediction [69–71]. Grad-CAM generates heatmaps that identify the most relevant regions for disease stage classification and diagnosis. Regions that are highly relevant for survival characteristics can also be localized. Some regions, particularly those with unique outlines, can be utilized for survival prediction and detection.

(2) **Genomics interpretability from deep learning.** Integrated gradient methods [72,73] are often used to interpret multi-omics data, such as genomics data. These methods examine how specific changes to original inputs can influence model outputs by calculating attention scores. In regression tasks such as survival prediction, attribution values indicate the magnitude and direction of the impact: positive attributions indicate an increase in predicted risk, while negative attributions indicate a decrease. In classification tasks, positive attribution increases the probability of a particular class, while negative attribution decreases it. This approach discovers molecular features that consistently contribute to model predictions in a group. The attribution value indicates the importance of features predicted by the model, where molecular features with high attribution values can serve as potential biomarkers for specific clinical applications. Identifying features with high average attribution values helps clinicians identify potential biomarkers important for differentiating clinical outcomes [47,74–76].

6. Challenges and future directions

The application of deep learning in radiology-genomics still faces many challenges, mainly caused by the increasing amount of multimodal data. Several previous reviews have discussed challenges such as fairness and data movement, as well as limited interpretability [3,77]. Here, we focus on four challenges specific to the integration and applications of radiology–genomics.

(1) **Modality missing in radiology-genomics integration.** A major challenge in integrating radiology and genomics is dealing with missing data, which may appear as partial or complete absence of one or more modalities [78,79]. Many existing multimodal deep learning models struggle to resolve missing data inputs given the limited availability of paired CT images and genomic sequencing datasets, i.e., CT images and genomic data from the same person poses a significant problem. This limitation often arises from different examination methods, associated costs and data privacy concerns. Noninvasive, cost-effective and time-efficient radiology is accessible to almost all patients. In contrast, high-throughput genomic sequencing, the predominant method for molecular profiling, is invasive, costly and time-consuming, and therefore inaccessible to some patients. The reliance on complete radiology-genomics data for model training limits the size of usable datasets, and the inability to utilize incomplete modalities despite their valuable information represents significant limitation [80]. It is crucial to develop multimodal deep learning models capable of handling missing input modalities in clinical applications.

(2) **Modality alignment in radiology-genomics integration.** Modality alignment refers to the process of harmonizing and integrating data from different sources [81–83]. In this scenario, radiology and genomics, which originate at the organismal and molecular levels respectively, and differ in scope and data distribution, are combined to create a unified analytical framework. This alignment is critical in multimodal studies as it ensures that data from each modality are accurately correlated and analyzed together [84,85]. When integrating radiology and genomics, modality alignment includes preprocessing steps such as normalization, registration, and feature selection, followed by the development of models that can effectively combine information from both modalities. Techniques such as canonical correlation analysis, multiview learning, and cross-modal learning are commonly used to match and integrate these different data sources [86,87]. Successful matching of modalities allows for more comprehensive and accurate interpretation of cancer features and leads to better diagnostic, prognostic and therapeutic outcomes.

(3) **Foundation model in radiology–genomics integration.** Recent advances in foundational models, such as natural language processing and computer vision, have demonstrated the potential of pretraining to learn the basic representation in the pretraining phase [88–90]. Due to extensive pretraining on multiple data sources, the obtained basic model can be used for downstream applications abroad. On the one hand, the imaging pretraining models, which are pretrained on large sets of labeled or unlabeled images, show improved performance compared to the baseline models in several clinical applications. RETFound [91] can improve the detection, diagnosis and prognosis of eye diseases through retinal imaging, while REMEDIS [92] mitigates such distribution performance issues and improves model robustness through a self-supervised representation learning strategy. On the other hand, the foundation model can learn molecular feature associations and gene regulation through pretraining on large genomics and mRNA data, improving predictions in network biology [92] and cell type annotation [93].

Foundation models have great potential to transform biomedicine and oncology. The integration of radiology and genomics into the foundation model should benefit multimodal analysis, learning new task and leveraging domain knowledge [94].

(4) **Integration of radiology-genomics with new omics.** In addition to the conventional genomics modality focused in radiology genomics, the integration of other new omics modalities is increasingly recognized as essential for the advancement precision oncology and would be called radiology-omics, taking into account considering transcriptomics [95], metabolomics [96] and deep pathomics [97,98] etc. Transcriptomics provides insights into gene expression patterns corresponding to various cancer hallmarkers [99], while metabolomics provides a detailed understanding of the metabolic alterations associated with cancer [100]. Deep pathomics, in which deep learning techniques are applied to histopathological images, can help reveal complex tissue architecture and cellular morphology [101–103]. Combining these more diverse omics data types with radiology genomics, i.e. radiology-omics, should enable a more comprehensive characterization of tumor heterogeneity and improve the accuracy of various clinical prediction tasks [104]. Multi-omics sample representation from multimodal learning can support various downstream clinical tasks with incomplete multi-omics datasets [104,105], further enhancing prognostic and predictive tasks with detailed clinical endpoints (e.g., cancer subtype or drug response prediction). Compared to single omics data used in conventional radiology-genomics studies (Table 3), integration with appropriate multi-omics data in various clinical applications can provide more comprehensive insights into cellular regulation and tumorigenesis according to the central dogma that will help identify potential new non-invasive candidate markers (Table 4).

Table 4
Radiology-genomics extension by integrating multiple levels of new omics data.

Omics data	Biological level	Information type	Clinical consideration
Genomics	DNA	Gene mutation marker (e.g. CNV)	Driver for cancer
Methylation	DNA	Epigenetic marker (e.g. CpG)	New environmental driver for cancer
Transcriptomics	RNA	Transcriptional regulation state	Biological status of cancer tissue
Metabolomics	Metabolite	Metabolic pathway activation state	Non-invasive metabolic markers from blood or tissue
Proteomics	Protein	Protein expression and functional state	Non-invasive functional markers from blood or tissue
Radiomics	Organ/ tissue	Organ imaging feature	Non-invasive pathogen markers from tissue although existing radiation exposure risk
Histology	Tissue/cell	Tissue architecture and cell morphology	Characterization of tumor heterogeneity

7. Conclusion

The integration of deep learning into radiology-genomics represents a transformative advance in the field of oncology [106,107]. This mini-review paper highlights the transformative impact of deep learning integration in radiology-genomics, a significant advance in oncology. The role of deep learning in harmonizing radiology and genomics is critical to advancing cancer diagnosis, treatment, and patient care. By correlating imaging and genetic data, these models provide deep insights into tumor characteristics, promoting personalized medicine. This integration significantly improves diagnostic precision, prognosis and treatment planning, setting a new standard in patient care. In particular, the ability to predict treatment responses and monitor disease progression in real time represents a major advance in compassionate and effective cancer treatment.

The choice of deep learning fusion method when integrating radiology and genomics data depends on the data properties, modality-specific information and general analysis goals. Each fusion approach has its strengths and considerations, and its effectiveness may vary depending on the specific challenges presented by the multimodal nature of radiology-genomics datasets. Ensuring the interpretability of radiology-genomic models is crucial for their successful use in clinical settings. This not only improves the understanding of model predictions, but also helps address concerns related to model reliability and potential impact on patient care. Transparent and interpretable AI models are more likely to be accepted and adopted in the medical community, contributing to better patient outcomes. These approaches and applications are intended to enable physicians to gain a deeper understanding of disease, ultimately leading to more effective and patient-centered healthcare practices.

As radiology-genomics continues to evolve, the increasing complexity and diversity of data will further emphasize the importance of AI. Advances in AI interpretability and adherence to ethical practices are critical to responsible use and maintaining the trust of patients and physicians. The fusion of radiology genomics and deep learning will revolutionize patient outcomes with focus on personalized, patient-centered care. This approach aims to not only extend life but also improve quality of life, representing a more effective, personalized and compassionate approach to cancer treatment. The journey of integration continues, and every step forward brings us closer to a future where cancer care is tailored to each individual patient.

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Author's contributions

TZ and YXL conceived and designed the study. FW performed analysis and wrote the original draft preparation. TZ reviewed and revised the manuscript. All authors have read and agreed to the published version of the manuscript.

CRediT authorship contribution statement

Tao Zeng: Writing – review & editing, Supervision, Conceptualization. **Feng-ao Wang:** Writing – original draft, Formal analysis, Data curation. **Yixue Li:** Resources, Project administration, Conceptualization.

Declaration of Competing Interest

All of the authors have no conflicts of interest to declare.

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