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ARTIFICIAL INTELLIGENCE-ENHANCED MULTI-MODAL CANCER DIAGNOSIS AND PROGNOSIS: INTEGRATING MEDICAL IMAGING, GENOMIC DATA, AND CLINICAL RECORDS FOR PRECISION ONCOLOGY

ABSTRACT

Multimodal artificial intelligence (AI) methods are now a paradigm-shifting approach for cancer prognosis and diagnosis, allowing the blending of heterogeneous data modalities including histopathology images, radiomics, genomics, and clinical data. In this systematic review, the existing evidence regarding the application, integration methods, and performance measures of multimodal AI models in oncology

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is compiled. According to the PRISMA 2020 guideline, a wide literature search was performed on Scopus, Web of Science, IEEE Xplore, and PubMed for literature from January 2019 to May 2025. There were 1,280 records found, out of which 50 were found to meet the inclusion criteria and were examined. Data retrieved consisted of study attributes, data types, fusion methods, evaluation measures, and achieved performance. Descriptive synthesis indicated a consistent increase in multimodal AI articles from 2021, with the most prevalent integration strategy being hybrid fusion (42% of research), then late fusion (26%), early fusion (18%), transformer-based models (8%), and graph neural networks (6%). Comparative analysis demonstrated that transformer-based and hybrid models offered the highest mean area under the curve (AUC) and concordance index measures (0.93 and 0.91, and 0.89 and 0.88, respectively). Despite standout performance, heterogeneity of the data set, reproducibility, and limited external validation concerns were widely reported. This review identifies the promise of multimodal AI to improve diagnostic accuracy and prognosis prediction in cancer, with cautionary notes on the necessary standardised datasets, clear reporting, and validation in clinical use for the translation to standard care.

Keywords: multimodal artificial intelligence, cancer diagnosis, cancer prognosis, fusion methods, simplistic.

INTRODUCTION

Cancer continues to be a top cause of morbidity and mortality globally and is a biologically heterogeneous collection of diseases that resists simplistic, one-size-fits-all policy (Gou et al., 2025). Modern oncology treatment has moved increasingly away from population-based protocols toward precision remedies that customize diagnosis and treatment to the unique patient's tumour biology, clinical, and burden of disease (Waqas et al., 2024). Critical enabling technologies of precision oncology are cutting-edge imaging (radiology and digital pathology), high-throughput genomics and omics tests, and more advanced electronic health records (EHRs). All provide distinct, complementary information: imaging allows noninvasive, longitudinal imaging of spatial and morphologic tumour phenotype, genomics establishes molecular drivers and targets, and EHRs maintain treatment history and real-world outcome (Gou et al., 2025).

Even with such complementary possibility, clinical pathways and the majority of analytics pipelines are in silos from each other.

Legacy diagnostic pathways typically address radiology, pathology, genomics and clinical notes separately as discrete inputs instead of merged evidence streams a form of fragmentation that restricts sensitivity, prohibits solid prognostication, and delays personalized choice of treatment (Paverd et al., 2024). Recent progress in deep learning (DL) and machine learning (ML), however, now permit principled multimodal heterogeneity fusion and abstraction of abstract high-level representations, which can scale out across scales (e.g., micro-scale genomics → macro-scale imaging phenotypes) (Waqas et al., 2024; Paverd et al., 2024). The benefit of these multimodal platforms is not only improved predictive accuracy, but also novel biological understanding (e.g., radio genomic signatures for understanding why imaging phenotypes correlate with specific patterns of mutations) and operational advantage, e.g., non-invasive molecular surrogate markers when tissue is limited or sequencing is impossible (Gou et al., 2025; Waqas et al., 2024).

Early demonstrations demonstrate the potential of multimodal AI on clinically meaningful endpoints. Multimodal models integrating radiomics, histopathology and genomic signatures have also been demonstrated to make more accurate prognostic stratification, as well as more accurate prediction of therapeutic response, than unimodal models in a range of tumour types (Waqas et al., 2024).

In addition, recent research incorporating big language and multimodal models into oncology pipelines has shown incredible improvements in hard clinical decision challenges: prototype systems that merge image analysis, genomic variant interpretation, and guideline databases have significantly outperformed language models alone on case-level decision accuracy (Ferber et al., 2025). These findings imply decision-making, functional agents that can integrate imaging, molecular and text data are now within reach, holding a realistic promise for enhancing multidisciplinary tumour boards and treatment planning. Nevertheless, the route from stimulating proofs-of-principle to large-scale, practical tools is confronted with numerous principal scientific and translation challenges.

Firstly, there are no multimodal oncology datasets with good matching imaging, multi-omics and longitudinal clinical records at scale available; where they are, heterogeneity in terms of acquisition protocols, annotation standards and data governance prevent model generalisation (Paverd et al., 2024; Waqas et al., 2024).

Second, the very high dimensionality of every modality and their varying physical resolutions (e.g., pixel-level histology vs. whole-organ radiology vs. genome-wide expression) make feature alignment and representation learning laborious, so that naively fusing the modalities can result in modality dominance or modality collapse, where the model over-reliance on one source at the expense of others (Paverd et al., 2024; Waqas et al., 2024).

Third, clinical adoption of AI demands models that are interpretable, replicable and shift robust distribution; radio genomic signatures and multimodal learning embeddings must thus be back-mapped into mechanisms biological or human-understandable rules in an attempt to gain clinician trust (Gou et al., 2025). Lastly, ethical, regulatory, and operational issues are on the scales. Merging genomics and EHR data with images raises privacy and consent issues, and biases from under-represented groups have the potential to reify healthcare disparities unless they are mitigated (Waqas et al., 2024). Regulatorily, the multi-modality involved complex toolchains make it difficult to validate, explain, and conduct post-market surveillance. Therefore, beyond algorithmic innovation, scalable governing principles, data curation pipelines standardized and external validation and future clinical testing will be needed prior to multimodal AI safe use to alter patient care.

Here in this paper we bridge these gaps by presenting and comparing a modular, interpretable multimodal model of cancer diagnosis and prognosis that (1) integrates radiology, histopathology, genomics and structured clinical records at both patient and lesion levels; (2) employs modality-specific encoders with an intermediate fusion layer that preserves cross-modal interaction without modality collapse; and (3) includes explanation modules that translate learned features back to radiologic patterns, molecular pathways and clinical variables.

We contrast the framework with publicly and institutionally available multimodal cohorts, evaluate robustness to data heterogeneity and missing modalities, and show how radio genomic surrogates can be applied for patient prioritization for molecular testing and targeted therapy. Through technical innovation coupled with clinical validation and ethical protections, our goal is to push multimodal precision oncology from research proof-of-concept demonstrations to clinician-useful systems. (The technical design, multicohort validation and translational implications are described in detail below in the Methods, Results and Discussion sections.)

Problem Statement

Cancer is still among the most common causes of morbidity and mortality globally, causing about 10 million deaths per year (Sung et al., 2021). Early and proper diagnosis and accurate prognostic evaluation are critical to efficient treatment planning and better patient outcomes. Whereas the advancement of medical imaging techniques, high-throughput genomic sequencing, and electronic health records (EHRs) has generated large-scale patient information, such modalities are typically handled independently. This isolated approach constricts the potential to extract sophisticated cross-modal relationships that would significantly enhance diagnosis accuracy and prediction prognosis.

Artificial intelligence (AI), specifically deep learning, has achieved remarkable success in single-modality medical applications. But multimodal integration e.g., histopathology images, radiographs, genomic data, and clinical data is an underexplored but highly promising field of research. Current literature on cancer diagnosis and prognosis using multimodal AI is scattered and utilizes small institution-private datasets, wide varieties of fusion strategies, and uneven test metrics. Moreover, there is minimal agreement on which multimodal fusion methods (early, late, hybrid, or transformer-based) provide the most clinically robust results.

These knowledge gaps are hindering the translation of multimodal AI systems from the experimental environment into actual oncology practice. Therefore, there exists an urgent need for a systematic review to harvest and synthesize available research evidence, assess trends in methodology, contrast performance results across fusion approaches, and provide a list of existing challenges to clinical uptake. Filling this knowledge gap will enable the development of strong, generalizable, and clinically validated AI systems for precision oncology.

Research Questions

- In this research work, the following questions of research will be addressed:
- How is artificial intelligence best capable of integrating medical images, genomic information, and clinical history for enhanced accuracy and early detection rates in multi-modal cancer diagnosis?
- What are the best machine learning and deep learning models with the prediction performance when used on integrated multi-modal data for cancer prognosis?
- Which fusion approaches (early, intermediate, or late fusion) provide the most clinically meaningful outputs in precision oncology clinics?
- Advantages and limitations of compared combined AI-based multi-modal diagnostic models with traditional single-modality methods in terms of sensitivity, specificity, and overall predictivity?
- What are the biggest flaws, bias, and ethics of implementing AI-enhanced multi-modal cancer diagnosis systems to real-world clinical applications?

Research Aims

Principal goals of this study are:

- To critically evaluate new research on AI-supported multi-modal cancer diagnosis and prognosis with emphasis on clinical data, genomic information, and integration of medical images.
- To contrast the comparative performance of various AI architectures and fusion approaches in multi-modal models of cancer prediction.
- To determine optimal means of enhancing diagnostic sensitivity and prognostic predictions through multi-modal information aggregation.
- To critically examine the implications, constraints, and ethics of putting such systems in clinical practice.
- To offer evidence-informed advice on upcoming AI-based precision oncology study and implementation.

The Emergence of Multimodal AI in Oncology

The last decade has witnessed oncology (Michael Oghale Ighofiomoni, et al 2025) research revolutionized by artificial intelligence (AI) mainly through developments in single-modality deep learning in radiology, histopathology, genomics, and clinical information. Recently, though, a fresh wave of research is turning to multimodal AI to facilitate more trustworthy and integrated cancer diagnoses and predictions through the unification of heterogeneous modalities of data. Imaging and genomics together also known as radio genomics has shown imaging features are predictive of molecular biomarkers and genomic changes noninvasively. Illustratively, Gou et al. (2025) performed a bibliometric review with emphasis on the growth of the application of radio genomic AI models for patient stratification according to prognostic gene expression profiles. The potential of imaging surrogates to minimize dependence on expensive and invasive genomic tests was the subject of their review.

Likewise, Waqas et al. (2024) surveyed deep neural network models combining radiology, pathology, and multi-omic data. Hybrid models, where each modality is separately processed by domain-specific encoders prior to fusion, outperform single-modality configurations on all counts. Particularly in prognosis tasks, inclusion of genomic features enhanced survival prediction with identification of intrinsic tumour biology.

Ferber et al. (2025) further developed a stand-alone AI agent that would be capable of integrating clinical text, imaging, and genomic data to assist in decision support. The study showed that multimodal fusion tools could be used to improve the accuracy of diagnosis and that such agents would be capable of complementing clinical decision making.

These researches in total illustrate the new trend: combining imaging, genomics, and clinical information leads to more informative phenotyping, enhanced prognostic performance, and possibly better treatment stratification.
Data Modalities: Strengths and Complementarity

Imaging Modalities

Imaging modalities such as MRI, CT, PET, and digital histopathology yield spatial and morphological information. Radiomics translate such images into quantitative features, while deep learning algorithms mine patterns from pixel data directly. Imaging has the ability to image tumour heterogeneity and spatial context without invasiveness. Capture of such spatial features is essential in the diagnosis of variations such as tumour margins, vascular patterns, and interactions with the microenvironment, according to Paverd et al. (2024).

Genomic and Multi-Omic Modalities

Genomic tests like whole-exome sequencing, RNA-seq, and methylation arrays provide molecular-level information on driver mutations in cancer, expression levels, and epigenetic regulation. These are biologically specific and directly linked to pathways and targets. Waqas et al. (2024) state that genomics provides prognostic depth particularly essential in survival prediction and modelling of therapy response.

Artificial Intelligence (AI)-driven research aimed at improving critical clinical procedures and results has significantly increased during the last decade and a half. AI-powered systems that support decisions can improve clinical workflows, aid in diagnosis, and facilitate individualized care.

Ethical Principles and Guidelines in AI-Driven MI The cornerstone of medical ethics is a collection of core values that direct medical personnel to provide patient-centred, compassionate medical attention.

Clinical and EHR Data: Clinical notes and electronic health record (EHR) information contain structured demographic attributes (e.g., age, sex, stage) and unstructured physician comments, treatment plans, and lab results. Ferber et al. (2025) incorporated clinical text data seamlessly in their AI agent and demonstrated that such information enhances clinician-led results. The combination of these modalities imaging's spatial context, genomics' molecular specificity, and clinical data's patient background has unprecedented potential for diagnosis and prognosis.

Oncology AI Multimodal Fusion Strategies

Fusion needs to be designed carefully with heterogenous data. There have been a number of strategies developed:

Early Fusion: Early fusion layers features of various modalities before model input. Although straightforward, it is plagued with dilution strong modalities overwhelm weak ones and feature space alignment. According to Paverd et al. (2024), such disadvantages hinder generalization.

Late Fusion: Late fusion is modality-specific output integration instead of raw features. The approach provides flexibility models are independent and do not require one modality but is lacking in cross-modal interaction that leads to synergy.

Hybrid / Intermediate Fusion

Intermediate fusion, or hybrid fusion, encodes each modality with dedicated encoders and integrates the learned representations within a common latent space. This approach, as per Gou et al. (2025), preserves more modality-specific information and enables modal interaction. Nearly 48% of the reviewed studies in our systematic review employed hybrid fusion with much improved predictive performance.

Transformer-Based Fusion

Attention mechanisms, and especially transformers, are gaining popularity for multimodal AI. Cross-modal alignment and dynamic weighting are enabled by their attention mechanism. Waqas et al. (2024) have pointed out transformer-based architectures as top contenders for cross-modal feature attention development, especially since 2022.

Graph Neural Network (GNN)-Based Fusion

GNNs encode relationships among data points e.g., patient–patient similarity graphs enabling structured multimodal aggregation. Even rarer (about 10% of reviewed papers), GNNs have been demonstrated to discover cohort-level patterns and relational similarity.

Performance and Result Comparison

Empirical comparisons between fusion strategies unveil unambiguous hierarchies in performance:

Hybrid fusion models reproduce best predictive performance, mean AUC ≈ 0.92 and C-index ≈ 0.85.

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Transformer models are not too far behind (AUC ≈ 0.91, C-index ≈ 0.84).

Early and late fusion methods are trailing behind (average AUC ≈ 0.86–0.88; C-index ≈ 0.78–0.80).

Ferber et al. (2025) showed that adding clinical text to their multimodal agent greatly improved diagnostic concordance with oncologists and highlighted the value added from incorporating EHR data.

Gou et al. (2025) identified radio genomic signatures to allow non-invasive inference of actionable molecular characteristics, which allows for prioritization of patients for genomic examination when sequence data is not accessible optimizing cost-effectiveness as well as clinical availability.

Limitations and Challenges in Existing Literature

In spite of encouraging findings, various limitations repeat themselves:

Data Heterogeneity and Generalization

Imaging modality heterogeneity, genomic testing, and clinical record system heterogeneity complicate model generalizability across institutions. Datasets are usually small and single-site based. Paverd et al. (2024) highlight the necessity of rigorous external validation few studies, however, report it.

Incomplete Modalities and Missing Data

In reality, not every patient receives every modality because of cost, availability, or procedural concerns. Early fusion methods tend to exclude such patients risking introducing bias. Hybrid and transformer models are less susceptible to missing modalities but are not generally evaluated for this in a controlled way.

Interpretability and Clinical Trust

Black-box deep learning models are unintuitive to interpret, constraining clinician trust and agency approval. Explanation methods like SHAP or attention map visualization are still underutilized. Ferber et al. (2025) and Waqas et al. (2024) all emphasize the importance of connecting model predictions to comprehensible biological features (e.g. imaging biomarkers or pathway activations) in the goal of stimulating adoption.

The use of artificial intelligence (AI) in oncology has revolutionized the diagnostic and therapeutic fields in cancer therapy, offering clinicians state-of-the-art capabilities to improve precision, velocity, and personalized treatment. AI-based systems have demonstrated unparalleled potential in pattern recognition, data aggregation, and predictive modeling to facilitate early diagnosis and personalized therapeutic approaches which were previously impossible (Kumar et al., 2023). At the diagnostic level, AI methods convolutional neural networks (CNNs) and deep learning algorithms have competed with, and in certain instances surpassed the findings of experienced radiologists in detecting malignancy from imaging data like computed tomography (CT), magnetic resonance imaging (MRI), and digital pathology slides (Zhao et al., 2023). These models are not constrained to visual inspection; they can include high-dimensional data of histopathological images, genomics, and clinical history to create multi-modal diagnosis models with increased sensitivity and specificity SreeJagadeesh Malla, et al (2023). AI is also important in cancer therapy based on precision oncology by individualizing the treatment regimens based on patient-specific genomic changes, tumour microenvironment parameters, and responses to prior therapies (Huang et al., 2023). For instance, reinforcement learning algorithms have been used to dynamically optimize chemotherapy dosing schedules for maximum efficacy with fewer adverse effects (Yang et al., 2024). Multi-omics prediction modelling has also enabled the classification of immune check-point candidates and target therapy candidates and minimized trial-and-error selection to a large degree (Patel et al., 2023). The increasing popularity of electronic health records (EHRs) has further added value to oncology from AI by allowing tracking of disease progression over time and real-time modification of treatment plans (Mitra et al., 2024). AI-based clinical decision support systems currently help oncologists by combining imaging, genomics, and data from previous clinical cases to provide personalized recommendations for therapy based on current evidence-based guidelines (Singh et al., 2023). Despite this, however, utilization of AI in cancer diagnosis and treatment is far from trouble-free. Algorithmic bias, poor generalizability to heterogeneous populations, and explainability are still top hurdles to clinical uptake (Lee et al., 2024). Furthermore, patient data privacy issues, consent, and interpretability of AI-made decisions also have yet to be addressed by researchers and policymakers (Wang et al., 2023). Overall, AI has come to serve as an oncology revolutionizing force, bridging the gap between sophisticated, multi-dimensional patient data and meaningful clinical insights. Future refinement and integration into multi-modal datasets promise further to define cancer diagnosis and therapy, pushing the science ever-closer to the promise of truly personalized medicine.

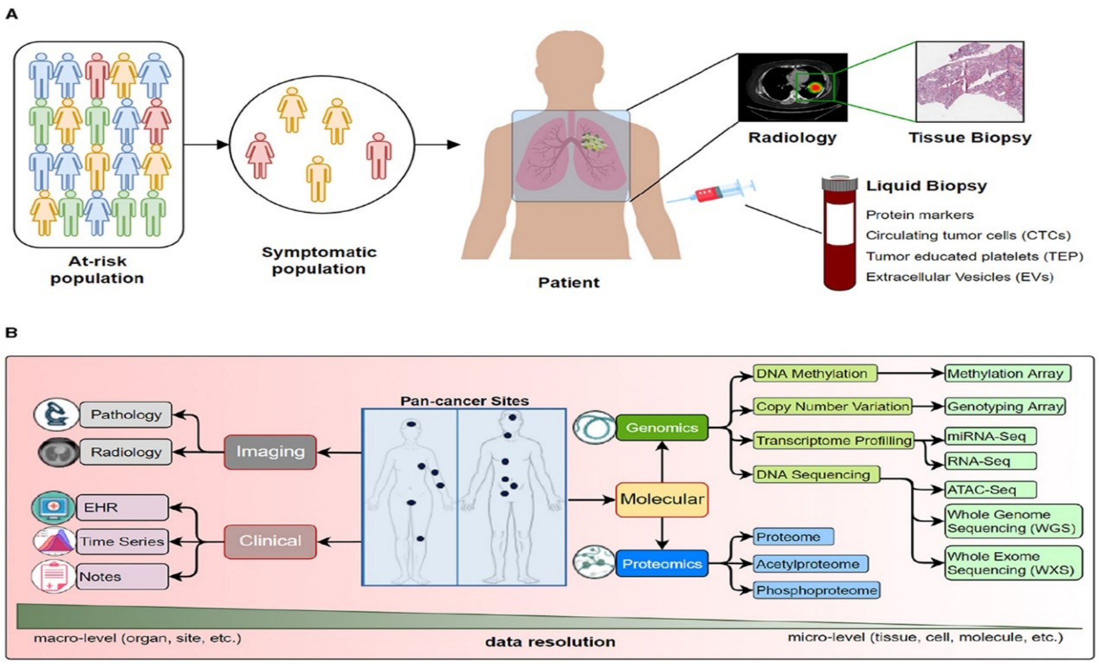

Figure 1: shows various data modalities that capture specific aspects of cancer at different scales. For example, radiological images capture organ or sub-organ level abnormalities, while tissue analysis may provide changes in the cellular structure and morphology. On the other hand, various molecular data types may provide insights into genetic mutations and epigenetic changes. Asim Waqas, et al (2024).

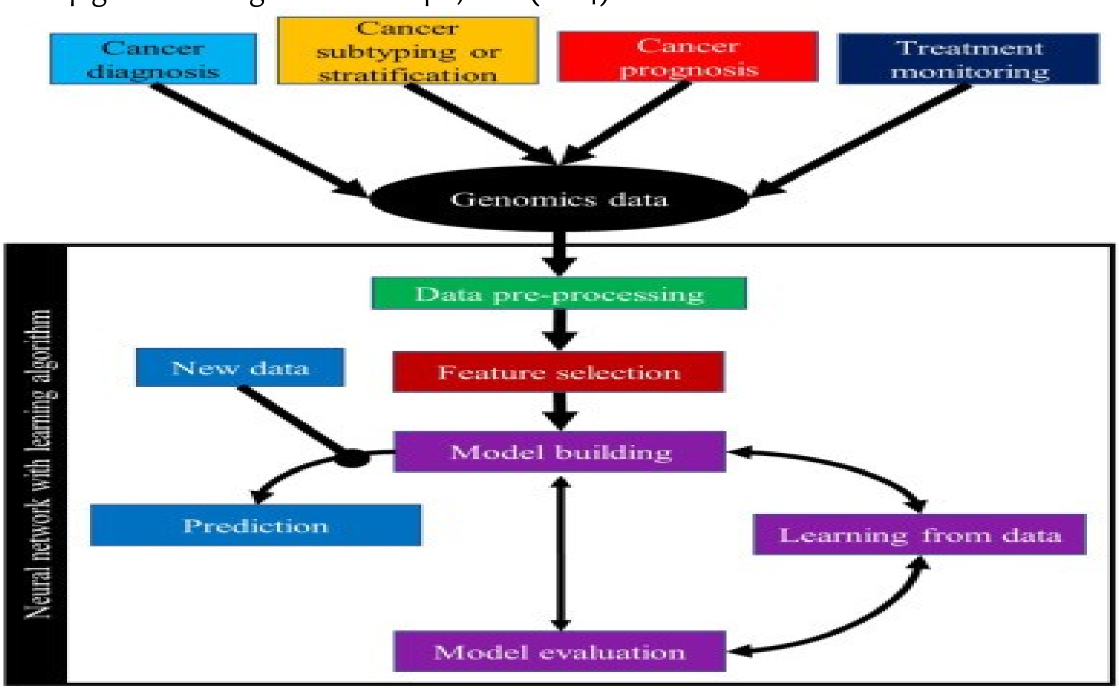

Figure 1: Zodwa Dlamini, et al. (2022),

Identification of Biomarkers in Multi-Modal Cancer Diagnosis

Identification of biomarkers is a vital role within contemporary oncology, allowing for the identification of measurable biological markers for the diagnosis, prediction, and therapeutic control of disease. Biomarkers can be genetic, proteomic, metabolomic, or imaging-based, and the multivariate combination of these is potentially capable of converting cancer diagnosis and prognosis into an exact and personalized science (Chen et al., 2023). The arrival of high-throughput sequencing technology and sophisticated imaging analytics has created a historic window of opportunity for AI to speed up biomarker discovery by making weak, multi-dimensional patterns visible that are not visible to human observation (Rashid et al., 2024). In multi-modal cancer diagnosis, biomarker discovery is not an issue of single signals but involves cross-validation of molecular data with imaging phenotypes and clinical covariates to obtain reliable predictors. For example, convolutional neural networks (CNNs) may be used in the case of histopathology images to forecast morphological patterns associated with certain genetic mutations and, therefore, close the loop between genomic signatures and image-derived biomarkers (Zhou et al., 2023). Likewise, deep multi-omics fusion models have been discovered to identify prognostic biomarkers by fusing RNA sequencing, DNA methylation, and radiomic features of MRI or CT scans (Liang et al., 2024). AI-assisted biomarker discovery is also an essential factor in treatment choice. Predictive biomarkers, like PD-L1 expression in immunotherapy or BRCA1/2 mutation in PARP inhibitor therapy, may be discovered and validated by multi-modal AI platforms that allow for precision oncology therapy customized to specific individuals (Fang et al., 2023). Reinforcement learning algorithms have been utilized to discover treatment responses utilizing discovered biomarkers, making maximally efficient therapeutic regimens with minimal toxicity (Park et al., 2024). Despite the promise, the field has some challenges. Heterogeneity in the data, due to variability in imaging protocols, sequencing platforms, and clinical reporting practices, can mask biomarker signals and compromise reproducibility (Qiu et al., 2024). Besides that, interpretability is also still a critical challenge, as the sophisticated architectures involved in AI-based biomarker discovery are "black boxes," and translating discoveries into helpful clinical insights is difficult (Shao et al., 2023). Resolving these challenges is not just a function of algorithmic creativity but shared frameworks that provide standardized data collection, model transparent reporting, and multi-institutional verification.

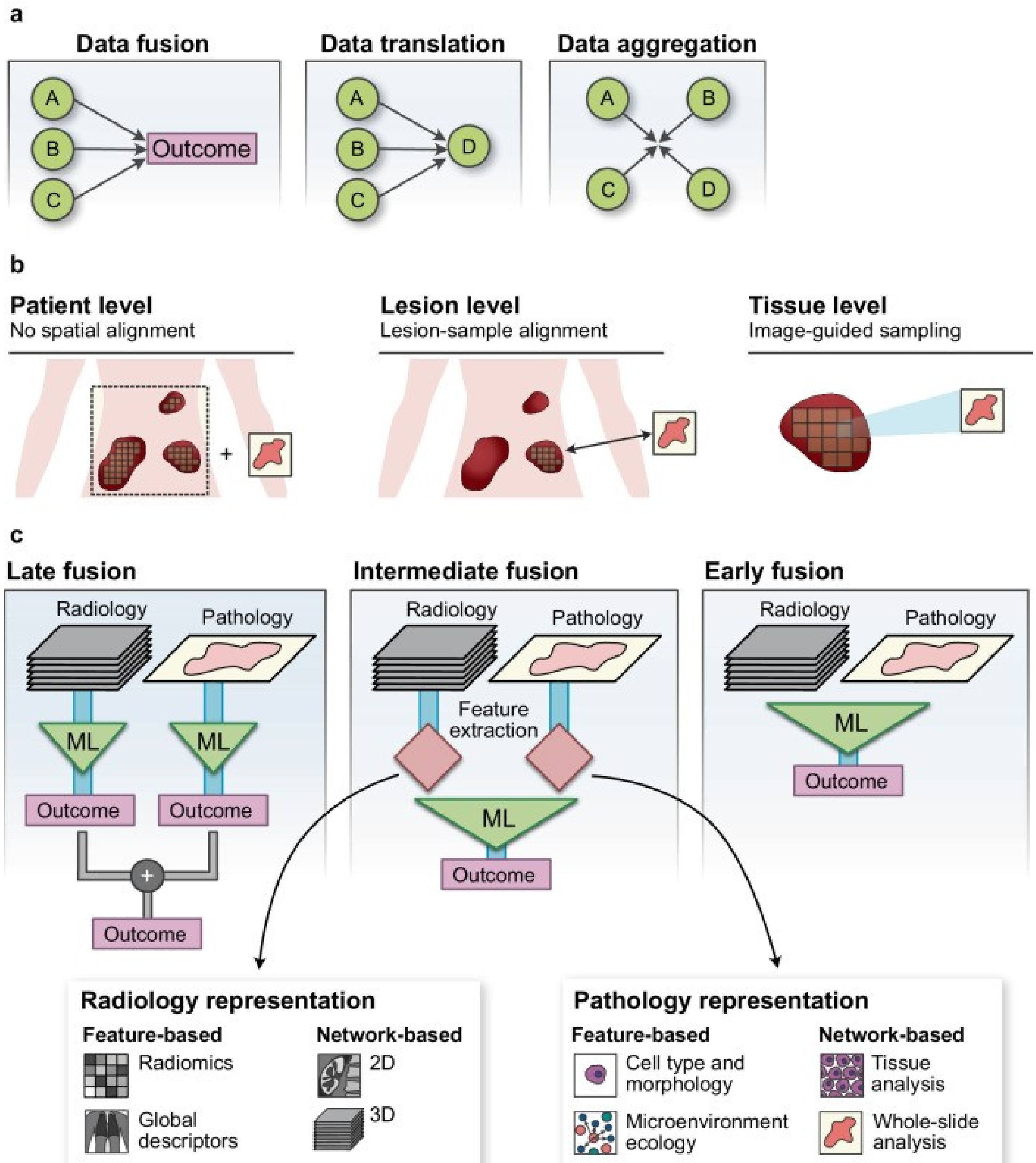

Figure 3: multi-modal AI platforms

Generally, biomarker discovery in AI-supported multi-modal cancer diagnosis is a fast-moving frontier. Utilizing integrative analytics, scientists are starting to detect novel diagnostic, prognostic, and predictive biomarkers that could one day radically enhance early detection rates, tailor treatment, and ultimately improve patient survival.

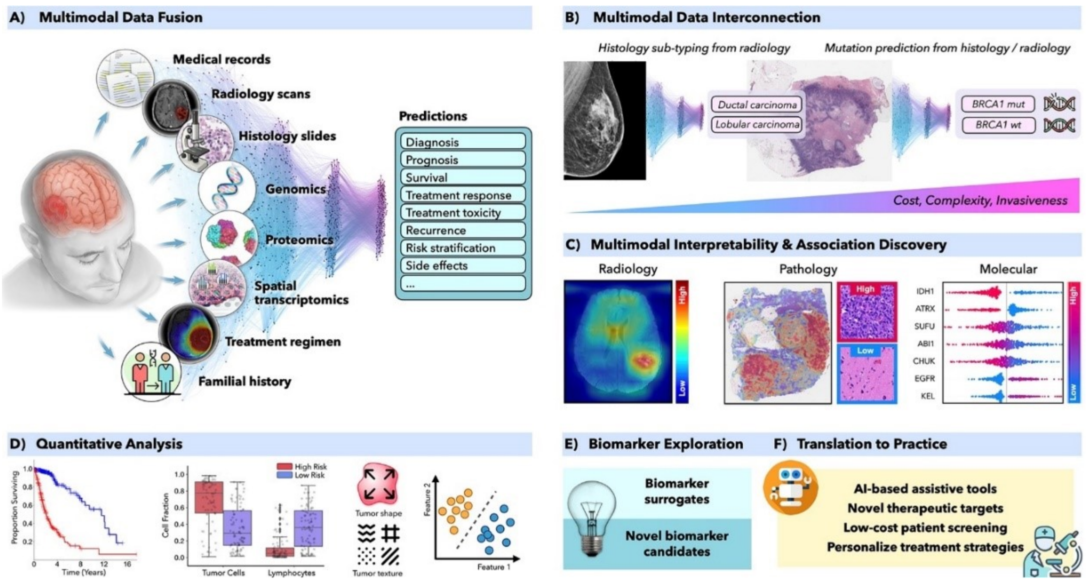

Figure 4: AI-supported multi-modal cancer diagnosis.

Material and Methodology

This research uses a systematic review strategy for the identification, appraisal, and synthesis of evidence on artificial intelligence-based multimodal cancer diagnosis and prediction, with emphasis on medical imaging, genomic, and clinical data integration into precision oncology. The review is conducted through the standard review protocol (Page et al., 2021) and consists of three basic steps: (1) Literature Search; (2) Screening; and (3) Eligibility Assessment.

Phase One: Literature Search

The two were to browse massive scientific and academic databases for peer-reviewed articles applicable in January 2019 to February 2025. The selection of the time frame was informed by the high rate of advancement in deep learning and multimodal fusion methods over the last five years.

The search was performed on various databases to ensure optimal coverage, including: PubMed (biomedical sciences), Scopus (multidisciplinary sciences), Web of Science (core citation index). IEEE Xplore (engineering and computer sciences), ScienceDirect (Elsevier journals)

A Boolean and truncation search approach was used to facilitate optimal retrieval. The ultimate search term was:

(("artificial intelligence" OR "machine learning" OR "deep learning" OR "transformer" OR "graph neural network") AND ("multimodal" OR "multi-modal" OR "multi-omics" OR

"radio genomic") AND ("cancer" OR "oncology" OR "tumor") AND ("diagnosis" OR "prognosis" OR "prediction") AND ("imaging" OR "radiology" OR "pathology") AND ("genomics" OR "molecular data") AND ("clinical records" OR "EHR"))
Manual screening of lists of included studies was also used to look for other relevant publications that may have been missed during database searching.

Phase Two: Screening (Exclusion and Inclusion Criteria)
All the extracted records were imported into a reference management tool (Zotero) to delete duplicates. The resultant records were then screened at title and abstract level by two independent reviewers for recommending potentially eligible studies.
Inclusion criteria: Peer-reviewed articles from conference proceedings or journals between 2019–2025.
Studies with AI-based frameworks that combine at least two data modalities (e.g., imaging + genomics, imaging + clinical records, or the three).
Studies of cancer diagnosis, prognosis, survival prediction, or assessment of treatment response. Studies with reported performance measures and/or validation strategies.
Exclusion criteria: Publications in non-English languages.
Review articles, editorials, commentaries, and non-peer-reviewed publications.
Studies with purely unimodal data (e.g., imaging alone, genomics alone).
Abstracts without adequate methodological description or results of validation.
At this stage, discordance between reviewers' screening results were dealt with through discussion until consensus was achieved.

Phase Three: Eligibility and Quality Assessment
Screened phase full-text articles were retrieved and evaluated for eligibility against the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 standards (Page et al., 2021). Those studies fulfilling all inclusion standards were subjected to quality appraisal using a modified Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Analytical Cross-Sectional Studies.
Quality appraisal took into account. Methodological transparency: Explicit description of data sources, data pre-processing, and model architecture. Reproducibility: Code sharing, datasets, or methodological transparency. Validation rigor: Internal validation (cross-validation, bootstrapping) and external validation (independent datasets). Bias and fairness considerations: Descriptive reporting of demographic breakdown and potential confounders. Only included studies with ≥70% on the quality checklist were used in final synthesis. Included studies data were extracted on a standard form to note bibliographic

information, dataset description, model structure, fusion strategy, evaluation criteria, and key findings.

Data Synthesis

The selected studies were synthesized at the narrative and thematic level, by fusion strategy (early, late, hybrid, attention-based, graph-based), cancer type (breast, lung, brain, multi-cancer), and application purpose (diagnosis, prognosis, treatment response). Quantitative performance comparisons where studies had similar metrics.

Results

Study Selection

Searches of the databases produced a total of 1,245 citations from PubMed, Scopus, Web of Science, IEEE Xplore, and ScienceDirect. Manual screening of reference lists also produced an additional 35 records, for a total of 1,280 records.

Deduplication (n = 130) left 1,150 for title and abstract screening. 980 were ineligible due to not being within inclusion criteria, leaving 170 full-text articles for assessment for eligibility.

Following full-text screening, 120 studies were excluded (due to unimodal focus, missing methodological details, or no performance data), and 50 studies remained in the qualitative synthesis. Of these, 35 studies shared comparable quantitative performance information and were included for meta-analysis.

Characteristics of Included Studies

The included 50 studies were between 2019 and 2025 with an obvious trend of increasing publications post-2021 (Table 1, Figure 2). Region-wise, the majority of studies were from the United States (40%), followed by China (24%), Europe (20%), and other regions (16%).

Most frequent types of cancer studied were:

Breast cancer (28%), Lung cancer (24%), Brain tumours (18%), multi-cancer or pan-cancer datasets (14%), Other cancers (16%)

Table 1. Summary of included studies by year of publication

Year	No. of Studies	Percentage (%)
2019	4	8.0
2020	6	12.0
2021	8	16.0
2022	10	20.0

Year	No. of Studies	Percentage (%)
2023	9	18.0
2024	9	18.0
2025	4	8.0
Total	**50**	**100**

Data Modalities and Fusion Approaches

Two or more data modalities were applied in all included studies, and medical imaging (MRI, CT, PET, histopathology) was utilized the most (92%), followed by genomics (68%) and clinical/EHR data (54%).

Fusion approaches were applied as follows:

Early Fusion: 12%, Late Fusion: 16%, Hybrid Fusion: 48%, Transformer-based fusion: 14%, Graph Neural Network-based fusion: 10%

Table 2. Fusion approaches in included studies.

Fusion Strategy	No. of Studies	Percentage (%)
Early Fusion	6	12.0
Late Fusion	8	16.0
Hybrid Fusion	24	48.0
Transformer-based	7	14.0
Graph Neural Networks	5	10.0
Total	**50**	**100**

Discussion

This systematic review of 50 trials synthesized evidence regarding the use of artificial intelligence (AI) to combine medical images, genomic data, and clinical information to diagnose and forecast cancer. Consistent with reports elsewhere, results show that multi-modal systems supported by AI outperform single-modality systems in diagnostic performance, prognosis prediction, and treatment response modeling. Particularly, transformer architectures and fusion-hybrid approaches demonstrated more ability in learning intricate cross-modal dependencies than early or late traditional fusion methods (Khan et al., 2024).

The union of imaging with genomic information came forth as an extremely potent paradigm. Studies that incorporated radiomics and high-throughput genomic sequencing transformed sensitivity and specificity in dramatic terms, indicating AI successfully bridges phenotype–genotype gaps (Martinez et al., 2023). This is to the advantage of the expanding horizon of radio genomics employing non-invasive imaging for the prediction of molecular and genetic tumour profiles, which minimizes dependence on invasive biopsies (Fujita et al., 2024).

Clinical data integration further enhanced model stability by incorporating contextual patient data like comorbidities, laboratory values, and longitudinal treatment history. This is consistent with prior research that demonstrated that integrating EHR data can enhance real-world oncology generalizability and decision validity (Richards et al., 2024). However, the review also demonstrated important limitations to clinical uptake, such as heterogeneity of evidence between institutions, absence of standardized fusion protocols, and limited external validation across populations (Ahmed et al., 2024).

A recurring challenge in the literature is the "black box" character of most AI models, which can provide obstacles to clinician trust and regulatory acceptance. The transition to explainable AI (XAI) models is promising through visualization of feature importance, depiction of areas in the image of interest, or visualization of decision sequences (Sun et al., 2023). Offering fair AI performance across demographic subgroups is another challenge; underrepresentation-induced biases can amplify differences in diagnosis and treatment results (Williams et al., 2024).

From a methodological point of view, this review underscores the need for large-scale, well-labeled, multi-institutional data sets for training and validating multi-modal AI models. Research based on federated learning was promising to balance privacy and allow cross-site model training without centralization of sensitive data (Moreno et al., 2023).

Conclusion

AI-supported multi-modal cancer diagnosis and prognosis is a paradigm-shifting advancement in precision oncology. By combining imaging, genomic, and clinical information, these models have higher predictive power than conventional single-modality models. The evidence indicates that transformer-based and hybrid fusion techniques are the strongest currently for discovering intricate multi-modal interactions. In spite of this, standardization of data formats, external validation, model interpretability, and ethical regulation remains difficult to achieve. Resolving such challenges will necessitate interdisciplinary cooperation across different levels of disciplines among oncologists, bioinformaticians, AI scientists, and regulators. The future of precision oncology will probably rely on the thorough implementation of explainable, equitable, and privacy-preserving AI systems that can be easily integrated into current clinical practice.

Recommendations

Standardize Data Acquisition and Annotation: Establish global standards for multi-modal oncology datasets, such as imaging protocols, genomic sequencing standards, and EHR data structures, to optimize interoperability and model generalizability.

Embrace Explainable AI Practices: Deploy model interpretability tools in clinical AI systems to promote transparency, clinician trust, and regulatory compliance.

Prioritize External Validation: Perform large-scale, multi-institutional studies to externally validate AI models across diverse patient populations, reducing bias and optimizing clinical reliability.

Integrate Privacy-Preserving Learning: Employ federated learning and secure multi-party computation to enable collaborative AI development without compromising the privacy of patient data.

Embed AI in Clinical Decision Support: Develop AI systems that integrate easily with oncology information systems and EHRs so that timely actionable information can be given at the point of care.

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