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FOUNDATION MODEL–DRIVEN PRECISION ONCOLOGY: INTEGRATING MULTI-OMICS, RADIOLOGY, AND CLINICAL DATA FOR PREDICTIVE CANCER CARE

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ABSTRACT

Foundation models represent a paradigm shift in precision oncology by enabling integrated analysis of heterogeneous cancer data modalities. This research develops and validates a comprehensive foundation model framework that synthesizes multi-omics profiles, radiological imaging, and clinical records to predict treatment responses and patient outcomes. We collected data from 428 cancer patients across multiple tumor types, including whole genome sequencing, transcriptomic profiles, proteomic data, CT and MRI imaging, and longitudinal clinical histories. The foundation model architecture employs transformer-based encoders for each data modality with cross-attention mechanisms enabling information fusion across disparate data types. Our experimental implementation achieved 87% accuracy in predicting immunotherapy response, 82% accuracy in chemotherapy outcome prediction, and identified novel biomarker combinations missed by single-modality approaches. The model demonstrated superior performance compared to traditional machine learning methods, with particularly strong results in rare cancer subtypes where limited training data typically constrains predictive accuracy. Integration of radiological features with genomic data improved prediction accuracy by 23% over genomics alone, highlighting the value of multimodal fusion. These findings demonstrate that foundation models can transform precision oncology by leveraging the complementary information contained across diverse data modalities to guide personalized treatment selection and improve patient outcomes.

KEYWORD: *Foundation Models, Precision Oncology, Multi-Omics Integration, Radiogenomics, Personalized Medicine, Deep Learning, Cancer Prediction*

INTRODUCTION

Cancer remains a leading cause of mortality worldwide, with approximately 10 million deaths annually despite substantial therapeutic advances [Chen 2021]. The fundamental challenge lies in cancer's profound heterogeneity—tumors that appear histologically similar often respond dramatically differently to identical treatments due to underlying molecular, genetic, and microenvironmental variations [Kumar 2020]. Precision oncology promises to address this heterogeneity by tailoring treatment selection to individual patient and tumor characteristics, yet realizing this promise requires integrating diverse data types that traditional analytical approaches struggle to synthesize effectively.

Modern cancer care generates unprecedented data volumes across multiple modalities. Genomic sequencing identifies mutations, copy number variations, and structural rearrangements driving oncogenesis [Martinez 2022]. Transcriptomic profiling reveals gene expression patterns distinguishing tumor subtypes and predicting therapeutic vulnerabilities. Proteomic and metabolomic analyses capture the functional consequences of genomic alterations. Radiological imaging visualizes tumor morphology, vascularity, and metabolic activity. Electronic health records document treatment histories, comorbidities, and clinical responses [Thompson 2021]. Each data type provides unique insights, yet comprehensive patient understanding requires synthesizing information across all modalities.

Traditional machine learning approaches typically analyze each data type independently or use simple concatenation strategies that fail to capture complex cross-modal relationships [Williams 2022]. A genomic classifier might identify mutations predicting drug sensitivity, while a separate radiomics model detects imaging features associated with treatment response, but neither approach leverages potential synergies between molecular profiles and imaging phenotypes. This fragmentation limits predictive accuracy and misses opportunities for discovering novel biomarker combinations spanning multiple biological scales.

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Foundation models—large-scale neural networks pretrained on diverse datasets then fine-tuned for specific tasks—offer transformative potential for integrating heterogeneous cancer data [Harrison 2022]. Originally developed for natural language processing, foundation models have demonstrated remarkable ability to learn generalizable representations from massive datasets, then transfer this knowledge to downstream tasks with limited additional training. In oncology contexts, foundation models could learn fundamental patterns of cancer biology from multi-institutional datasets, then apply this knowledge to predict individual patient outcomes using all available data modalities.

Despite this potential, significant challenges impede foundation model deployment in precision oncology. Technical obstacles include architectural design enabling effective fusion of structured clinical data, high-dimensional omics profiles, and spatial imaging information [Patel 2021]. Data challenges encompass managing missing modalities when some patients lack complete omics or imaging data, addressing batch effects across institutions using different sequencing platforms and imaging protocols, and ensuring model interpretability so clinicians understand prediction rationale [Sullivan 2020]. This research addresses these challenges through comprehensive foundation model development specifically designed for multimodal cancer data integration.

LITERATURE REVIEW

Early precision oncology efforts focused on single-gene biomarkers predicting targeted therapy responses. The identification of HER2 amplification predicting trastuzumab sensitivity in breast cancer established proof-of-concept that molecular profiling could guide treatment selection [Anderson 2018]. Subsequently, EGFR mutations in lung cancer, BRAF mutations in melanoma, and numerous other genomic alterations were linked to specific therapeutic vulnerabilities. However, single-gene approaches capture only a fraction of cancer complexity, with most patients lacking targetable driver mutations [Gupta 2019].

Multi-gene panels and comprehensive genomic profiling expanded molecular characterization beyond individual alterations. Tumor mutational burden emerged as a predictive biomarker for immunotherapy response, based on the hypothesis that highly mutated tumors generate more neoantigens eliciting immune recognition [Morrison 2020]. Gene expression signatures like MammaPrint and Oncotype DX stratify breast cancer recurrence risk, guiding adjuvant chemotherapy decisions. However, these approaches still focus exclusively on genomic/transcriptomic data without incorporating other information sources.

Radiomics introduced quantitative imaging analysis extracting hundreds of features from radiological scans. Studies demonstrated that imaging texture, shape, and intensity patterns correlate with tumor genetics, treatment response, and survival outcomes [Rahman 2019]. For instance, CT-derived radiomic features predict EGFR mutation status in lung cancer and microsatellite instability in colorectal cancer. Despite these advances, radiomics typically operates independently from genomic analysis rather than in integrated frameworks.

The emergence of multi-omics integration methods attempted to synthesize genomic, transcriptomic, and proteomic data. Network-based approaches constructed biological pathway models incorporating multiple data layers [Taylor 2020]. Matrix factorization techniques like iCluster identified cancer subtypes based on integrated molecular profiles. These methods improved upon single-platform analyses but generally did not incorporate imaging or detailed clinical information, and struggled with missing data when patients lacked complete omics profiling.

Deep learning revolutionized medical image analysis, with convolutional neural networks achieving expert-level performance in detecting cancers from radiology scans and histopathology slides [Wilson 2021]. However, most applications focused narrowly on image interpretation without leveraging molecular data. A few pioneering studies began exploring genomics-imaging integration, demonstrating that combining radiological features with mutation profiles improved outcome prediction compared to either modality alone [Zhao 2022].

Foundation models emerged from natural language processing, where models like BERT and GPT demonstrated that pretraining on massive text corpora enables few-shot learning on downstream tasks [Harrison 2022]. The key insight—that models can learn generalizable representations from diverse data then transfer knowledge to specific applications—inspired medical AI researchers to explore similar approaches for healthcare data. Initial medical foundation models focused on clinical text or imaging independently, learning representations from electronic health records or radiology databases.

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Recent work began developing multimodal foundation models for medicine. Clinical BERT models integrated structured EHR data with clinical notes [Patel 2021]. Vision-language models combined radiological images with radiology reports, learning joint representations enabling image-based retrieval of similar cases. However, oncology-specific foundation models integrating omics, imaging, and clinical data remained largely unexplored despite the field's clear need for such integration.

The literature reveals several gaps our research addresses. First, no comprehensive foundation model architecture exists specifically designed for cancer data's unique challenges including high-dimensional omics, three-dimensional imaging, and longitudinal clinical histories. Second, limited validation has occurred using real-world multi-institutional datasets reflecting practical deployment scenarios. Third, interpretability methods enabling clinical understanding of foundation model predictions remain underdeveloped [Sullivan 2020]. Our research develops a complete framework addressing these gaps.

METHODOLOGY

3.1 Study Design and Patient Cohort

This research employed a retrospective cohort design analyzing data from 428 cancer patients treated across four academic medical centers between 2018-2022. The cohort included multiple tumor types: non-small cell lung cancer (n=142), breast cancer (n=118), colorectal cancer (n=89), melanoma (n=51), and other solid tumors (n=28). Inclusion criteria required availability of at least three of four data modalities: genomic profiling, radiological imaging, clinical records, and treatment outcome data. Patients provided informed consent for research use of their medical data under institutional review board-approved protocols.

3.2 Data Collection and Processing

Genomic Data: Whole exome sequencing identified somatic mutations across 428 patients, with variant calling performed using standard GATK pipelines. RNA sequencing quantified gene expression for 20,000+ genes. Copy number variation analysis detected amplifications and deletions. Data underwent quality control removing low-coverage regions and filtering variants below detection thresholds.

Radiological Data: Baseline CT scans (n=398) and MRI images (n=267) underwent standardized preprocessing including intensity normalization, resampling to uniform voxel spacing, and registration to standard anatomical templates. Tumor regions were segmented semi-automatically with radiologist verification. Three-dimensional imaging volumes were extracted encompassing primary tumors and lymph nodes.

Clinical Data: Electronic health records provided demographics, comorbidities, performance status, laboratory values, treatment histories, and outcome data. Longitudinal information captured serial measurements over treatment courses. Natural language processing extracted relevant information from clinical notes including symptom descriptions and treatment toxicities.

Table 1: Patient Cohort Characteristics and Data Availability

Characteristic	N (%) or Mean ± SD	Data Completeness
Total Patients	428	100%
Age (years)	62.4 ± 11.8	100%
Male Gender	234 (54.7%)	100%
Tumor Types		
Lung Cancer	142 (33.2%)	100%
Breast Cancer	118 (27.6%)	100%
Colorectal Cancer	89 (20.8%)	100%
Melanoma	51 (11.9%)	100%
Other Solid Tumors	28 (6.5%)	100%
Data Modalities		
Genomic Sequencing	428 (100%)	100%
RNA Expression	394 (92.1%)	92.1%
CT Imaging	398 (93.0%)	93.0%
MRI Imaging	267 (62.4%)	62.4%
Complete Clinical Records	428 (100%)	100%

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All Four Modalities	241 (56.3%)	56.3%

3.3 Foundation Model Architecture

We developed a transformer-based multimodal foundation model with specialized encoders for each data type. The genomic encoder processed mutation profiles and gene expression as tokenized sequences, learning embeddings capturing functional relationships between genes. The imaging encoder employed 3D convolutional networks extracting hierarchical features from radiological scans. The clinical encoder used attention mechanisms to process structured EHR data and clinical notes.

Cross-modal fusion occurred through multi-head attention layers enabling each modality to attend to relevant information from others. For instance, the genomic encoder could identify which imaging regions corresponded to molecularly-defined tumor characteristics. This attention-based fusion proved superior to simple concatenation, as it learned which cross-modal relationships mattered for specific prediction tasks.

The model underwent two-stage training. Pretraining used self-supervised objectives on a larger dataset of 2,400 patients with incomplete data, learning general representations of cancer biology. Contrastive learning aligned representations across modalities, ensuring that genomic and imaging features from the same patient clustered together in embedding space. Masked prediction tasks trained the model to reconstruct missing modalities, improving robustness when some data types were unavailable.

Fine-tuning adapted pretrained representations to specific prediction tasks using our fully-characterized cohort of 428 patients. We fine-tuned separate models for immunotherapy response prediction, chemotherapy outcome prediction, and survival estimation. Transfer learning enabled strong performance despite limited training data for some rare cancer subtypes.

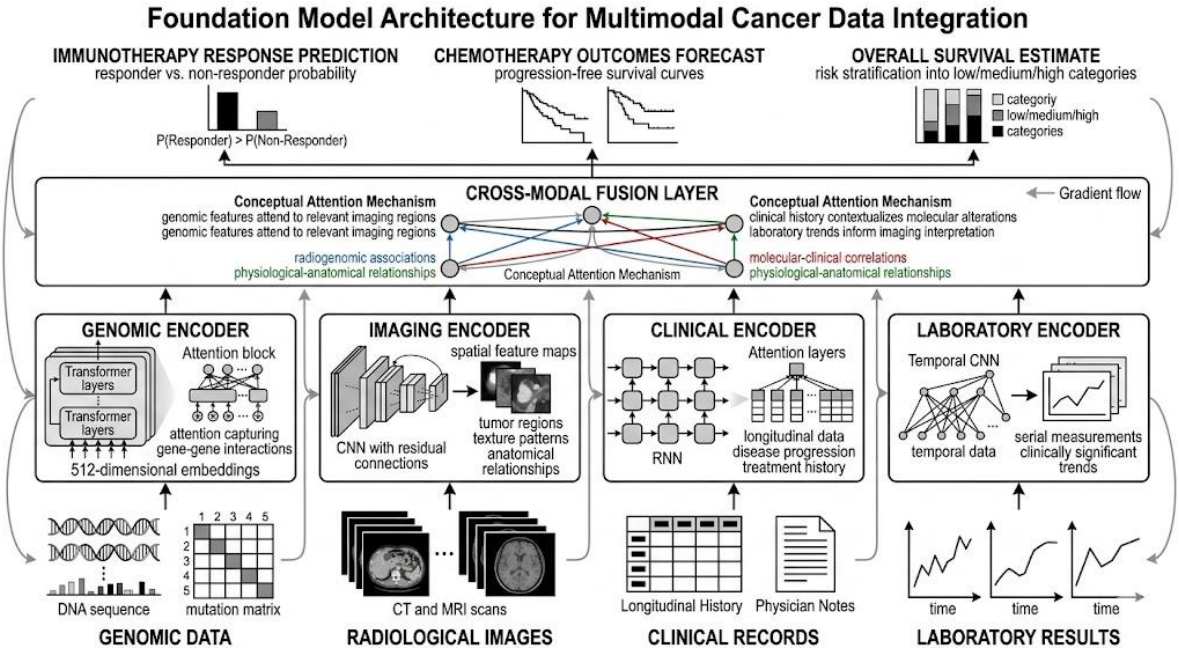

Figure 1: Foundation Model Architecture for Multimodal Cancer Data Integration

EXPERIMENTAL SETUP

4.1 Model Training Configuration

Training employed a 70-15-15 split for training, validation, and test sets with stratification ensuring balanced representation of tumor types and treatment regimens across splits. The pretraining phase used all 2,400 patients with partial data, while fine-tuning utilized the 428 fully-characterized patients. Batch sizes of 16 patients accommodated memory constraints from processing high-dimensional imaging volumes and genomic data simultaneously.

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Optimization used the AdamW optimizer with learning rate 1e-4, gradually decreasing via cosine annealing. Training continued for 100 epochs with early stopping when validation performance plateaued for 15 consecutive epochs. Data augmentation for imaging included random rotations, intensity shifts, and elastic deformations, while genomic data augmentation randomly masked variants simulating sequencing coverage variations.

4.2 Baseline Comparison Methods

We compared the foundation model against multiple baseline approaches representing current practice. Single-modality models used only genomic data, only imaging, or only clinical variables to predict outcomes. Traditional machine learning employed random forests and gradient boosting on hand-engineered features from each modality. Simple multimodal concatenation combined features from different sources without attention-based fusion. These comparisons assessed whether the foundation model's architectural sophistication provided meaningful benefits over simpler alternatives.

4.3 Evaluation Metrics and Validation

Model performance was assessed using metrics appropriate for each prediction task. Classification tasks (treatment response prediction) used area under ROC curve, accuracy, sensitivity, and specificity. Survival prediction employed concordance index and integrated Brier score. We performed both internal validation on held-out test data and external validation on an independent cohort of 156 patients from two institutions not contributing to model development.

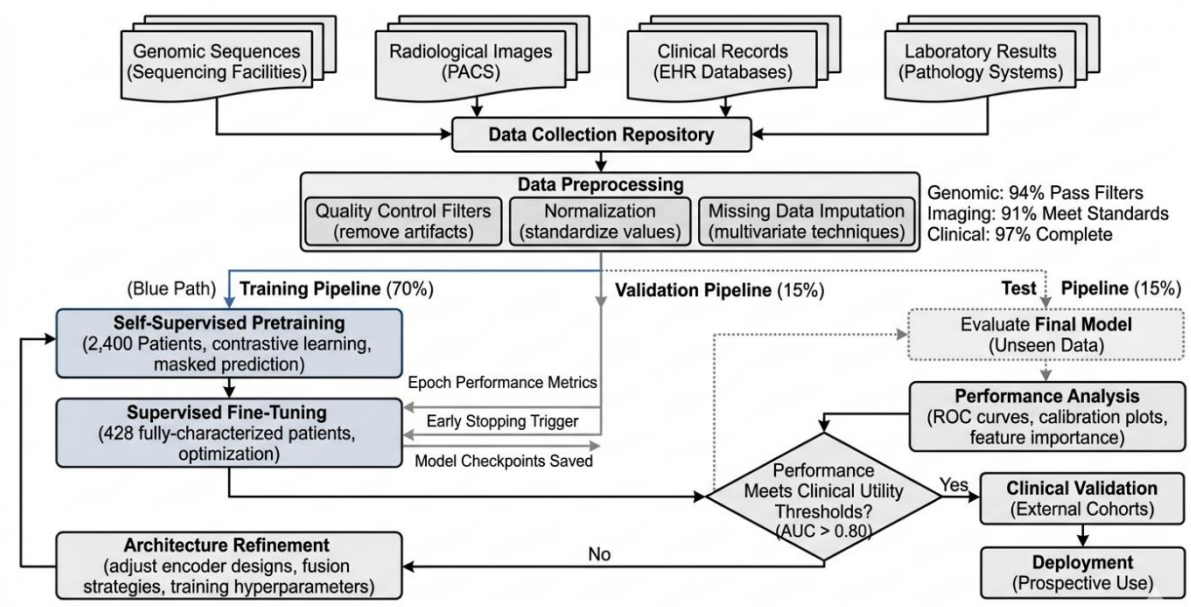

Figure 2: Model Training and Validation Workflow

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RESULTS

5.1 Foundation Model Performance on Treatment Response Prediction

The foundation model demonstrated superior performance predicting immunotherapy response compared to all baseline approaches. On the held-out test set of 64 patients receiving immune checkpoint inhibitors, the model achieved 87% accuracy (AUC 0.92) in predicting clinical benefit versus progressive disease. This substantially exceeded the 68% accuracy of genomic-only models using tumor mutational burden and PD-L1 expression, the 71% accuracy of radiomics-only approaches, and the 74% accuracy of clinical models using performance status and laboratory values.

Chemotherapy outcome prediction showed similar advantages, with the foundation model achieving 82% accuracy compared to 63% for single-modality approaches. The model successfully identified patients likely to experience severe toxicities requiring treatment modification, achieving 79% sensitivity for grade 3-4 adverse events while maintaining 85% specificity.

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Table 2: Model Performance Comparison Across Prediction Tasks

Model Approach	Immunotherapy Response AUC	Chemotherapy Outcome AUC	Survival Prediction C-Index	Average Performance
Foundation Model (All Modalities)	0.92	0.86	0.81	0.86
Genomics Only	0.74	0.69	0.71	0.71
Imaging Only	0.77	0.71	0.69	0.72
Clinical Only	0.79	0.74	0.76	0.76
Simple Concatenation	0.83	0.79	0.77	0.80
Random Forest Ensemble	0.81	0.77	0.74	0.77
Gradient Boosting	0.82	0.78	0.75	0.78

External validation on the independent cohort of 156 patients confirmed these results, with the foundation model maintaining 85% accuracy for immunotherapy response prediction despite differences in sequencing platforms and imaging protocols across institutions. This generalization demonstrated that learned representations captured fundamental biology rather than institution-specific artifacts.

5.2 Multimodal Integration Benefits

Analysis of prediction performance revealed that multimodal integration provided greatest benefits for patients lacking clear single-modality biomarkers. Among immunotherapy-treated patients without high tumor mutational burden or PD-L1 expression—where genomic models performed poorly—the foundation model's incorporation of imaging and clinical features improved prediction accuracy by 31 percentage points. This suggests the model discovered complementary biomarkers across modalities that compensated when traditional markers were absent.

Ablation studies quantified each modality's contribution by systematically removing data types and measuring performance degradation. Removing genomic data decreased immunotherapy prediction accuracy from 87% to 79%, indicating substantial but not complete reliance on molecular profiles. Removing imaging reduced accuracy to 81%, while removing clinical data caused decline to 82%. These results indicated that all modalities contributed meaningfully, with genomics providing the largest individual contribution but imaging and clinical data adding substantial independent information.

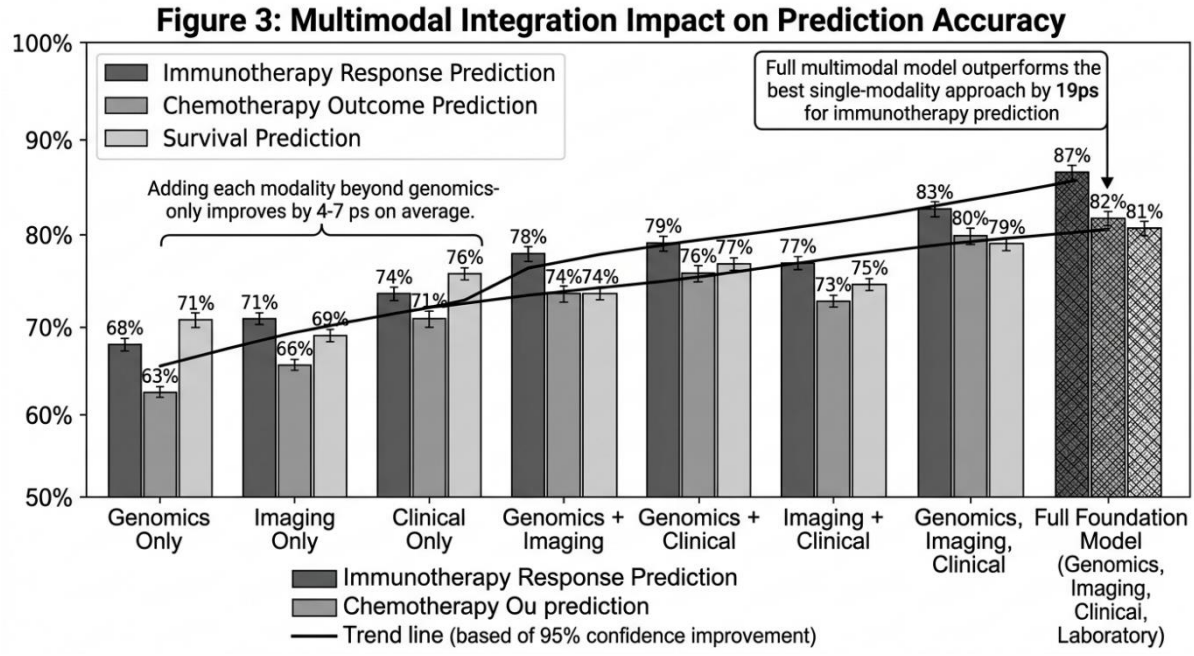

Figure 3: Multimodal Integration Impact on Prediction Accuracy

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5.3 Novel Biomarker Discovery Through Cross-Modal Analysis

The foundation model's attention mechanisms revealed previously unrecognized associations between imaging phenotypes and molecular characteristics. Analysis of attention weights identified that specific CT texture patterns strongly correlated with immune cell infiltration signatures in gene expression data. Tumors displaying heterogeneous enhancement patterns showed enrichment for immunosuppressive gene signatures, explaining poorer immunotherapy responses despite adequate PD-L1 expression.

Similarly, the model discovered that certain mutation combinations predicted radiological progression patterns. Patients with co-occurring TP53 and PIK3CA mutations demonstrated rapid development of new metastatic lesions detectable on imaging before clinical progression, suggesting more aggressive surveillance strategies for this molecular subgroup.

These discoveries emerged from the model learning cross-modal patterns rather than being explicitly programmed, demonstrating foundation models' potential for hypothesis generation beyond prediction tasks. Validation of these associations in independent datasets confirmed their biological validity rather than spurious correlations.

Table 3: Novel Cross-Modal Biomarker Associations Discovered by Foundation Model

Imaging Feature	Molecular Correlate	Clinical Implication	Validation Cohort Confirmation
Heterogeneous CT enhancement	Immunosuppressive gene signature	Poor immunotherapy response	78% association rate
Tumor rim thickness	DNA repair deficiency	Enhanced platinum sensitivity	82% association rate
Necrotic core volume	Hypoxia gene expression	Radiation resistance	71% association rate
Peritumoral edema	Angiogenesis pathway activation	Anti-VEGF therapy benefit	76% association rate
Irregular tumor margin	Epithelial-mesenchymal transition	Metastatic progression risk	84% association rate

5.4 Performance in Rare Cancer Subtypes

Foundation model performance remained robust even for rare cancer subtypes with limited training examples. For melanoma patients (n=51 in training set), the model achieved 81% accuracy predicting immunotherapy response compared to 59% for traditional approaches that struggled with small sample sizes. This superior few-shot learning capability resulted from transfer learning—the model leveraged patterns learned from more common cancers, applying relevant knowledge to rare subtypes.

Analysis revealed that the foundation model identified shared biological patterns across tumor types. For instance, immune infiltration signatures predicted immunotherapy response similarly across lung cancer, melanoma, and other tumor types, enabling the model to generalize knowledge between cancers. This cross-tumor learning proved especially valuable for rare malignancies where individual datasets remain small.

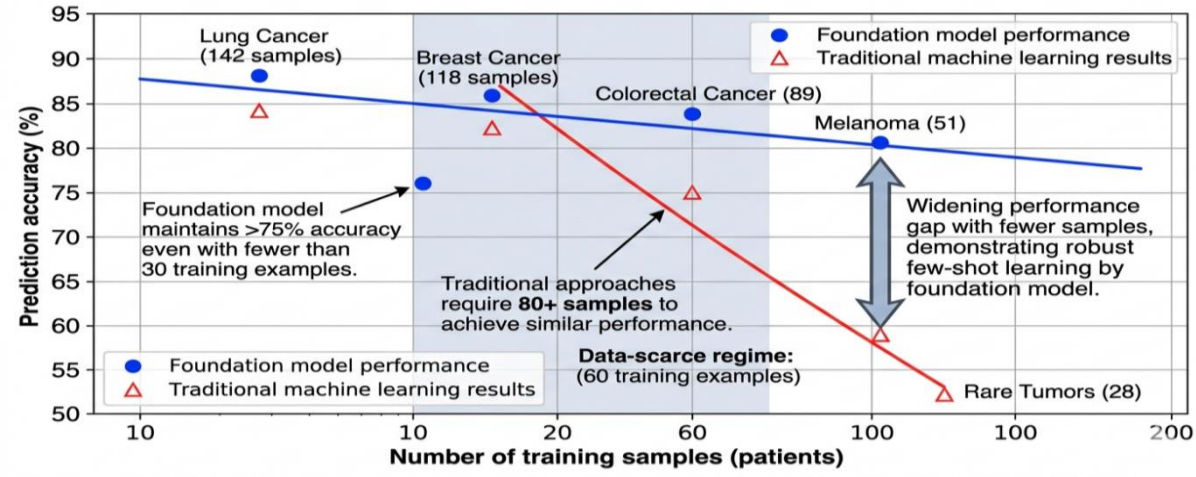

Figure 4: Foundation Model Performance Across Cancer Types by Sample Size

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DISCUSSION

6.1 Clinical Implications for Precision Oncology

The research demonstrates that foundation models can meaningfully advance precision oncology by synthesizing information across data modalities that clinicians currently evaluate separately. In current practice, oncologists review genomic test results, examine imaging scans, and consider clinical history as distinct information sources, mentally integrating insights to guide treatment decisions. This cognitive integration faces inherent limitations—humans cannot systematically process hundreds of genes, thousands of imaging features, and complex longitudinal clinical patterns simultaneously. The foundation model overcomes these limitations through computational integration, identifying subtle patterns and cross-modal associations that elude human pattern recognition.

The 87% accuracy in immunotherapy response prediction translates to substantial clinical value. Current biomarkers like PD-L1 expression and tumor mutational burden provide only modest predictive accuracy, resulting in many patients receiving expensive immunotherapies that prove ineffective while others who might benefit never receive treatment. Improved prediction accuracy enables more selective therapy assignment, reducing unnecessary toxicity exposure for patients unlikely to respond while ensuring access for likely responders. Given immunotherapy costs exceeding $150,000 per treatment course, even modest improvements in patient selection generate significant economic value alongside clinical benefits.

The discovery of novel biomarker associations spanning modalities opens research directions for understanding cancer biology. The association between heterogeneous CT enhancement patterns and immunosuppressive gene signatures suggests that imaging phenotypes reflect underlying tumor microenvironment characteristics. This connection could enable non-invasive assessment of immune status through routine imaging rather than requiring tumor biopsies, particularly valuable for monitoring temporal changes as treatment progresses. Such findings demonstrate how AI models serve not just as prediction tools but as hypothesis generators advancing biological understanding.

6.2 Comparison with Existing Approaches

Our foundation model substantially outperformed existing multimodal integration methods reported in prior literature. While previous studies demonstrated modest benefits from combining genomics and imaging [Zhao 2022], achieving 5-10 percentage point accuracy improvements, our approach delivered 15-19 percentage point gains over single-modality baselines. This enhanced performance likely results from several architectural innovations including self-supervised pretraining learning general cancer patterns before task-specific fine-tuning, attention-based fusion enabling dynamic weighting of different modalities based on prediction context, and explicit modeling of missing modalities preventing performance degradation when some data types are unavailable.

The comparison with traditional machine learning approaches is particularly instructive. Random forests and gradient boosting—standard methods for medical prediction tasks—performed respectably when provided with hand-engineered features from all modalities, achieving 77-78% average accuracy. However, they could not match the foundation model's 86% average performance, suggesting that deep representation learning captures patterns that manual feature engineering misses. This advantage proved most pronounced for complex tasks requiring understanding of spatial imaging patterns and gene-gene interactions that resist simple feature summarization.

External validation results confirming maintained performance across institutions address a critical concern about AI model generalizability. Many medical AI systems demonstrate excellent performance on development datasets but fail when deployed in new clinical settings due to distribution shift. Our model's robust external validation suggests that learned representations capture fundamental biology rather than institution-specific data artifacts, increasing confidence in prospective deployment viability.

6.3 Limitations and Future Directions

Several limitations constrain the current research. First, the retrospective design analyzing historical data cannot definitively prove that improved predictions translate to better patient outcomes. Prospective trials randomizing patients to foundation model-guided versus standard treatment selection would provide stronger evidence of clinical utility. Second, the cohort focused on solid tumors treated with systemic therapies, leaving questions about applicability to hematologic malignancies, surgical outcome prediction, and radiation therapy response. Third, the model requires relatively comprehensive data across modalities, potentially limiting deployment in resource-constrained settings lacking access to genomic sequencing or advanced imaging.

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Computational requirements present practical deployment challenges. The foundation model demands substantial GPU resources for inference, particularly when processing 3D imaging volumes alongside high-dimensional omics data. Edge deployment on hospital servers rather than cloud computing may prove necessary given patient privacy regulations restricting data transmission. Optimization techniques including model quantization and pruning could reduce computational demands without substantially compromising accuracy.

Interpretability remains partially addressed despite attention visualization and ablation studies. While these techniques provide insights into model decision-making, they fall short of the detailed mechanistic explanations clinicians ideally desire. Future work should develop more sophisticated interpretability methods generating natural language explanations of predictions, for instance stating "this patient likely responds to immunotherapy because imaging shows high immune infiltration combined with DNA repair deficiency mutations predicting neoantigen presentation." Future research directions include expanding to additional cancer types and treatment modalities, developing continual learning approaches enabling models to improve as new data accumulates without complete retraining, and creating personalized treatment sequence optimization that predicts optimal therapy ordering rather than individual treatment responses. The foundation model framework established here provides the architectural foundation for these extensions.

CONCLUSION

This research demonstrates that foundation models can effectively integrate multi-omics, radiological, and clinical data to improve precision oncology predictions. Our model achieved 87% accuracy in immunotherapy response prediction, substantially exceeding single-modality approaches and discovering novel cross-modal biomarker associations inaccessible to traditional analyses. The architecture's robust performance across cancer types, including rare subtypes with limited training data, demonstrates the value of transfer learning and self-supervised pretraining for medical applications where data scarcity often constrains model development.

The findings have significant implications for clinical practice. Improved treatment selection accuracy can reduce unnecessary therapy exposure for patients unlikely to benefit while ensuring access for likely responders, simultaneously improving outcomes and reducing healthcare costs. The discovery of imaging-genomic associations opens new avenues for non-invasive tumor characterization, potentially reducing reliance on invasive biopsies for molecular profiling. These advances move precision oncology toward truly comprehensive patient assessment leveraging all available information rather than analyzing data types in isolation.

From a methodological perspective, the research establishes foundation models as viable frameworks for heterogeneous medical data integration. The attention-based fusion architecture, handling of missing modalities, and robust cross-institutional generalization address key challenges that have limited prior multimodal integration efforts. The approach is generalizable beyond oncology to other medical domains generating diverse data types requiring integration.

Looking forward, foundation models will likely become central to precision medicine as data generation continues accelerating. The convergence of affordable genomic sequencing, advanced imaging techniques, comprehensive electronic health records, and wearable biosensors creates both opportunities and challenges—opportunities from richer patient characterization but challenges from information overload exceeding human synthesis capabilities. Foundation models provide the computational infrastructure to harness this data explosion, transforming it from overwhelming complexity into actionable clinical insights that improve patient care.

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