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Review Article

Radiomics and Machine Learning for Predicting Immunotherapy Response in Solid Tumors

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Immunotherapy, particularly immune checkpoint inhibitors (ICIs), has transformed the treatment landscape for numerous solid tumors, including non-small cell lung cancer (NSCLC), melanoma, renal cell carcinoma, hepatocellular carcinoma, and urothelial carcinoma. Despite remarkable clinical successes, only a subset of patients derives durable benefit, highlighting the need for reliable predictive biomarkers. Current biomarkers such as programmed death-ligand 1 (PD-L1) expression, tumor mutational burden (TMB), and microsatellite instability (MSI) demonstrate limited predictive accuracy and are constrained by spatial and temporal tumor heterogeneity. Radiomics has emerged as a promising non-invasive approach capable of extracting quantitative imaging biomarkers that capture intratumoral heterogeneity and the tumor microenvironment. Concurrent advances in machine learning have enabled the development of predictive models that integrate radiomic, clinical, pathological, and molecular data for individualized response prediction. Recent studies have demonstrated that radiomics-based machine learning models can predict immunotherapy response, durable clinical benefit, progression-free survival, and overall survival across multiple solid tumors. Furthermore, emerging approaches such as delta-radiomics, radiogenomics, deep learning, and multimodal learning are expanding the predictive capabilities of imaging biomarkers. However, substantial challenges remain, including lack of standardization, limited external validation, reproducibility concerns, small datasets, and regulatory barriers. This review critically examines the biological rationale underlying immunotherapy response prediction, discusses methodological foundations of radiomics and machine learning, evaluates current evidence across major solid tumors, and explores future opportunities involving foundation models, federated learning, and multi-omics integration. The convergence of radiomics, artificial intelligence, and precision oncology has the potential to significantly improve patient selection for immunotherapy and facilitate personalized cancer treatment strategies.

Keywords: Radiomics; Machine learning; Immunotherapy; Immune checkpoint inhibitors; Precision oncology; Radiogenomics; Artificial intelligence; Solid tumors.

INTRODUCTION

Cancer remains one of the leading causes of morbidity and mortality worldwide, accounting for millions of new diagnoses and deaths annually. Advances in molecular biology and cancer immunology have led to the development of immunotherapeutic strategies that harness the host immune system to recognize and eliminate malignant cells [1]. Among these approaches, immune checkpoint inhibitors targeting programmed cell death protein-1 (PD-1), programmed death-ligand 1 (PD-L1), and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) have demonstrated unprecedented clinical benefits across diverse solid tumors, including NSCLC, melanoma, renal cell carcinoma, hepatocellular carcinoma, and urothelial carcinoma [2,3]. Despite these advances, treatment responses remain highly variable. While some patients experience durable responses and prolonged survival, others derive minimal benefit or develop rapid disease progression. Consequently, accurate prediction of immunotherapy response has become a major priority in precision oncology [4]. Existing biomarkers such as PD-L1 expression, TMB, MSI, and tumor-infiltrating lymphocytes (TILs) provide valuable information but exhibit important limitations related to sampling bias, spatial heterogeneity, temporal variability, and inconsistent predictive performance across tumor types [5]. Medical imaging is routinely performed throughout the cancer care continuum and offers a unique opportunity to assess entire tumor burdens non-invasively. Traditional radiological assessment primarily relies on qualitative interpretation and size-based response criteria. However, medical images contain vast amounts of quantitative information that are not readily discernible by human observers [6]. Radiomics has emerged as a transformative approach that converts standard medical images into high-dimensional quantitative data. Through computational extraction of shape, intensity, texture, and higher-order features, radiomics provides objective characterization of tumor phenotype and heterogeneity [7]. The integration of radiomics with machine learning algorithms enables identification of complex imaging patterns associated with treatment response, prognosis, and molecular characteristics [8]. Recent investigations have increasingly focused on applying radiomics and machine learning to predict immunotherapy outcomes. Several studies have reported encouraging predictive performance for response assessment, survival prediction, hyperprogression detection, and identification of durable clinical benefit [9,10]. Moreover, advances in deep learning, radiogenomics, and multimodal artificial intelligence are facilitating integration of imaging with genomic, pathological, and clinical information to improve predictive accuracy [11]. This review examines the biological basis of immunotherapy response, discusses methodological foundations of radiomics and machine learning, critically evaluates current evidence regarding response prediction across major solid tumors, and explores future directions for integrating imaging biomarkers into precision immuno-oncology.

2. Biological Basis of Immunotherapy Response

The effectiveness of immunotherapy depends on complex interactions between tumor cells, immune cells, stromal components, and molecular signaling pathways within the tumor microenvironment (TME). Understanding these biological mechanisms is essential for developing predictive biomarkers capable of identifying patients most likely to benefit from treatment [12]. The TME comprises a heterogeneous ecosystem of malignant cells, immune cells, fibroblasts, endothelial cells, cytokines, and extracellular matrix components. Among these elements, tumor-infiltrating lymphocytes play a particularly important role in mediating antitumor immune responses. High densities of activated CD8+ cytotoxic T cells have consistently been associated with favorable responses to immune checkpoint blockade and improved survival outcomes [13]. The PD-1/PD-L1 signaling pathway represents one of the most extensively studied immune regulatory mechanisms. PD-1 is expressed on activated T cells, whereas PD-L1 may be expressed by tumor cells and immune cells within the TME. Engagement of PD-1 with PD-L1 suppresses T-cell activation and promotes immune evasion. Monoclonal antibodies targeting PD-1 or PD-L1 restore antitumor immunity and have become standard therapies for multiple malignancies [14]. Similarly, CTLA-4 functions as a negative regulator of T-cell activation during the early stages of immune responses. Inhibition of CTLA-4 enhances T-cell proliferation and activation, contributing to improved antitumor immunity. Combination blockade of PD-1 and CTLA-4 has demonstrated superior efficacy in selected cancer types but is associated with increased toxicity [15]. Tumor mutational burden has emerged as another important biomarker because highly mutated tumors generate larger numbers of neoantigens capable of stimulating immune recognition. Several studies have reported associations between elevated TMB and improved response to checkpoint inhibitors; however, predictive performance remains inconsistent across cancer types [16]. Likewise, MSI-high tumors exhibit increased neoantigen loads and generally demonstrate favorable responses to immunotherapy [17]. Nevertheless, no single biomarker adequately captures the complexity of immunotherapy response. Tumors frequently exhibit profound spatial and temporal heterogeneity, with variations in immune cell infiltration, genomic alterations, metabolic activity, and microenvironmental characteristics occurring within different tumor regions and over time [18]. Consequently, tissue-based biomarkers obtained from limited biopsy samples may fail to represent the entire disease burden. Radiomics offers a potential solution by enabling non-invasive assessment of whole-tumor heterogeneity and immune-related phenotypes. Emerging radiogenomic studies suggest that quantitative imaging features may correlate with immune signatures, T-cell infiltration patterns, PD-L1 expression, and other biologically relevant characteristics [19]. These observations provide a strong biological rationale for developing imaging-based biomarkers capable of predicting immunotherapy response. Although considerable progress has been achieved, significant challenges remain regarding biomarker standardization, validation, and clinical implementation. Future predictive frameworks will likely require integration of multiple complementary biomarkers rather than reliance on any single parameter [20].

3. Fundamentals of Radiomics and Machine Learning

Radiomics is a quantitative imaging analysis methodology that transforms medical images into mineable high-dimensional data. The underlying premise is that imaging phenotypes reflect biological processes occurring within tumors and their microenvironment. By extracting quantitative features from routinely acquired imaging studies, radiomics seeks to identify biomarkers associated with diagnosis, prognosis, molecular characteristics, and therapeutic response [7]. A typical radiomics workflow begins with image acquisition. Computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) are the most commonly utilized modalities in immunotherapy research. Image quality and acquisition parameters significantly influence feature reproducibility, making standardization an important consideration [21]. The second step involves tumor segmentation, which defines regions of interest for analysis. Segmentation may be performed manually, semi-automatically, or automatically using artificial intelligence techniques. Variability in segmentation remains a major source of uncertainty in radiomics studies and can substantially affect downstream model performance [22]. Following segmentation, quantitative features are extracted. Shape features characterize tumor geometry and morphology. First-order features describe voxel intensity distributions without considering spatial relationships. Texture features capture intratumoral heterogeneity through matrices such as the gray-level co-occurrence matrix and gray-level run-length matrix. Wavelet features provide multiscale characterization of image patterns and often enhance predictive performance [23]. Because radiomics datasets frequently contain hundreds or thousands of features, feature selection is essential to reduce dimensionality and minimize overfitting. Common techniques include least absolute shrinkage and selection operator (LASSO), recursive feature elimination, minimum redundancy maximum relevance, and mutual information-based methods [24]. Machine learning algorithms subsequently use selected features to construct predictive models. Logistic regression remains widely employed because of its simplicity and interpretability. Random forests effectively model nonlinear relationships and demonstrate robustness to noisy data. Support vector machines are particularly useful for high-dimensional datasets, whereas gradient boosting methods such as XGBoost frequently achieve superior predictive performance in radiomics applications [25]. Deep learning represents a major evolution beyond conventional machine learning. Unlike handcrafted radiomics approaches, deep neural networks automatically learn hierarchical imaging representations directly from raw data. Convolutional neural networks have shown promising results for immunotherapy response prediction, although their clinical implementation remains limited by data requirements and interpretability concerns [26]. Model validation is critical for ensuring clinical reliability. Internal validation techniques such as cross-validation provide preliminary performance estimates, whereas external validation using independent cohorts represents the gold standard for assessing generalizability [27]. Unfortunately, many published radiomics studies lack rigorous external validation, limiting clinical translation. To address concerns regarding transparency, explainable artificial intelligence approaches have gained increasing attention. Methods such as SHAP (Shapley Additive Explanations), LIME (Local Interpretable Model-Agnostic

Explanations), saliency maps, and attention mechanisms facilitate interpretation of model predictions and may enhance clinician trust [28]. Radiomics and machine learning collectively provide a powerful framework for extracting clinically meaningful information from medical images. However, successful implementation requires standardized methodologies, robust validation strategies, and integration with biological and clinical knowledge to ensure reproducibility and clinical utility [29,30].

4. Radiomics for Predicting Immunotherapy Response

The rapid expansion of immune checkpoint inhibitors (ICIs) has generated substantial interest in developing reliable biomarkers capable of predicting treatment response. While tissue-based biomarkers such as PD-L1 expression and tumor mutational burden provide important biological information, they often fail to capture the spatial and temporal heterogeneity of solid tumors. Radiomics has emerged as a promising non-invasive biomarker platform capable of characterizing the entire tumor burden through quantitative analysis of medical imaging data [31]. By integrating radiomic features with machine learning algorithms, investigators have developed predictive models for treatment response, durable clinical benefit, survival outcomes, hyperprogression, and pseudoprogression across multiple tumor types [32].

Non-Small Cell Lung Cancer

Non-small cell lung cancer (NSCLC) represents the most extensively studied malignancy in radiomics-based immunotherapy research because immune checkpoint inhibitors have become standard treatment options for advanced disease. Despite significant improvements in survival associated with anti-PD-1 and anti-PD-L1 therapies, only a subset of patients experiences durable clinical benefit [33]. One of the landmark studies in this field was conducted by Sun et al., who developed a CT-based radiomic signature associated with CD8-positive T-cell infiltration. Their multicenter investigation demonstrated that radiomic features reflecting intratumoral heterogeneity correlated with immune phenotypes and predicted response to anti-PD-1/PD-L1 therapy [34]. Importantly, the radiomic biomarker showed superior predictive performance compared with several conventional clinical variables. Subsequent studies have further demonstrated that CT-derived radiomic signatures can predict objective response, progression-free survival, and overall survival in NSCLC patients receiving immunotherapy [35]. Several machine learning models integrating radiomic features with clinical characteristics have achieved area-under-the-curve (AUC) values exceeding 0.75, highlighting the potential clinical utility of imaging biomarkers [36]. A particularly important application involves prediction of durable clinical benefit. Durable responders often exhibit distinct radiomic phenotypes characterized by increased heterogeneity and specific texture patterns, suggesting that imaging may capture biologically relevant features associated with immune activation [37].

Melanoma

Melanoma has historically served as a model disease for immunotherapy development. Checkpoint inhibitors targeting CTLA-4 and PD-1 have substantially improved outcomes in advanced melanoma, yet response heterogeneity remains a major challenge [38]. Radiomics investigations in melanoma have primarily focused on CT and PET/CT imaging. Quantitative imaging features associated with metabolic activity, lesion heterogeneity, and tumor burden have demonstrated significant correlations with treatment outcomes [39]. Several studies have reported that radiomic signatures outperform conventional response assessment metrics for predicting progression-free survival and overall survival following immunotherapy [40]. PET-based radiomics has shown particular promise because metabolic alterations frequently precede anatomical changes. Texture features derived from fluorodeoxyglucose positron emission tomography (FDG-PET) images have been associated with immune-related treatment response and long-term survival outcomes [41]. These findings suggest that radiomics may facilitate earlier identification of responders and non-responders compared with conventional imaging criteria.

Renal Cell Carcinoma

The treatment landscape of metastatic renal cell carcinoma (RCC) has been transformed by immune checkpoint inhibitors and combination immunotherapy regimens. However, reliable predictive biomarkers remain limited [42]. Recent radiomics studies have demonstrated associations between CT-derived imaging features and immunotherapy outcomes in RCC. Models incorporating tumor heterogeneity, vascular characteristics, and morphological descriptors have shown promising predictive performance for treatment response and survival [43]. Furthermore, radiomic analyses have suggested potential correlations between imaging phenotypes and underlying immune microenvironment characteristics, including T-cell infiltration and immune-related gene expression profiles [44]. Compared with traditional clinical risk models, radiomics-based approaches may provide more individualized risk stratification. Nevertheless, most available studies remain retrospective and involve relatively small patient cohorts, underscoring the need for prospective validation [45].

Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) presents unique challenges because of underlying liver disease, complex tumor biology, and substantial heterogeneity in treatment responses. Immunotherapy-based regimens have become increasingly important in advanced HCC management, creating demand for predictive biomarkers [46]. Radiomics investigations have demonstrated that CT- and MRI-derived features can predict response to immune checkpoint blockade in HCC. Several studies reported associations between radiomic signatures and progression-free survival, objective response rates, and overall survival [47]. Features reflecting vascular architecture, intratumoral heterogeneity, and peritumoral tissue characteristics appear particularly informative. An emerging area of interest involves evaluation of the peritumoral microenvironment. Studies have suggested that radiomic features extracted from tissue surrounding the tumor may provide additional predictive information regarding immune infiltration and treatment responsiveness [48]. Such findings highlight the importance of considering the broader tumor ecosystem rather than focusing exclusively on intratumoral regions.

Head and Neck Squamous Cell Carcinoma

Head and neck squamous cell carcinoma (HNSCC) has demonstrated meaningful responses to immune checkpoint inhibitors, particularly in recurrent and metastatic settings. However, response rates remain modest, emphasizing the need for predictive biomarkers [49]. Radiomics studies in HNSCC have reported associations between imaging features and immunotherapy outcomes. CT- and PET-based radiomic signatures have shown predictive value for objective response, progression-free survival, and overall survival [50]. Several investigations have also explored relationships between radiomic features and PD-L1 expression, revealing potential imaging correlates of immune-related biomarkers. Compared with conventional clinical variables, machine learning models integrating radiomics and clinical data have generally demonstrated superior predictive performance. Nonetheless, considerable variability exists among studies regarding imaging protocols, feature extraction methods, and validation strategies, limiting direct comparison of results [51].

Urothelial Carcinoma

Immune checkpoint inhibitors have become important treatment options for advanced urothelial carcinoma. However, only a minority of patients achieve durable responses, creating substantial interest in predictive biomarker development [52]. Recent radiomics studies have demonstrated that CT-derived texture and heterogeneity features can predict immunotherapy outcomes in urothelial carcinoma. Machine learning models combining radiomic and clinical variables have shown encouraging performance for identifying responders and predicting survival outcomes [53]. Moreover, radiomics may facilitate assessment of treatment-related changes that precede measurable alterations in tumor size. Although evidence remains relatively limited compared with NSCLC and melanoma, preliminary findings support further investigation of imaging biomarkers in urothelial carcinoma populations [54].

Colorectal Cancer

Immunotherapy has demonstrated remarkable efficacy in mismatch repair-deficient and microsatellite instability-high colorectal cancers, whereas responses in microsatellite-stable disease remain limited [17]. Consequently, identifying predictive biomarkers capable of refining patient selection is of considerable clinical importance. Radiomics investigations have reported associations between imaging features and MSI status, immune infiltration, and immunotherapy responsiveness [55]. Several machine learning models have successfully predicted MSI status using CT imaging, raising the possibility of non-invasive identification of patients most likely to benefit from checkpoint inhibition [56]. Recent studies have also explored radiomic signatures associated with treatment outcomes in metastatic colorectal cancer. Although evidence remains less extensive than for other tumor types, early findings suggest that quantitative imaging biomarkers may contribute to precision immunotherapy strategies [57].

Prediction of Durable Clinical Benefit, Hyperprogression, and Pseudoprogression

Beyond conventional response prediction, radiomics has shown promise for addressing unique challenges associated with immunotherapy. Durable clinical benefit represents one of the most clinically meaningful outcomes because long-term responders often experience substantial survival advantages [58]. Multiple studies have demonstrated that baseline radiomic signatures can identify patients likely to achieve prolonged disease control. Hyperprogressive disease, characterized by accelerated tumor growth following immunotherapy initiation, remains poorly understood and difficult to predict. Emerging evidence suggests that radiomic features reflecting aggressive tumor biology and heterogeneity may help identify patients at risk for hyperprogression before treatment initiation [59]. Similarly, pseudoprogression poses a significant diagnostic challenge because transient increases in tumor size may mimic disease progression despite favorable therapeutic responses. Preliminary studies indicate that radiomics and machine learning approaches may improve differentiation between true progression and pseudoprogression by analyzing complex imaging patterns beyond simple size measurements [60]. Collectively, current evidence suggests that radiomics provides valuable information regarding immunotherapy response across multiple solid tumors. Although methodological heterogeneity and limited external validation remain important challenges, radiomics-based biomarkers consistently demonstrate potential to complement existing molecular and clinical predictors. Future multicenter studies incorporating standardized methodologies and prospective validation will be essential for translating these promising findings into routine clinical practice.

5. Machine Learning Models for Immunotherapy Prediction

The increasing availability of radiomic data has stimulated widespread application of machine learning (ML) techniques for predicting immunotherapy outcomes. Machine learning algorithms can identify complex, nonlinear relationships among imaging biomarkers, clinical characteristics, molecular variables, and treatment responses that may not be discernible through conventional statistical methods [41]. As a result, ML-based predictive models have become central to contemporary precision immuno-oncology research.

Supervised Learning Approaches

Supervised learning remains the most commonly employed strategy in radiomics-based immunotherapy prediction. Logistic regression, support vector machines (SVMs), random forests, and gradient boosting algorithms have been extensively applied to classify responders and non-responders to immune checkpoint inhibitors [42]. Logistic regression offers simplicity, interpretability, and robustness, making it attractive for clinical implementation. However, its ability to capture complex nonlinear interactions is limited. In contrast, SVMs effectively handle high-dimensional radiomic datasets and often demonstrate superior classification performance in relatively small cohorts [43]. Random forests and gradient boosting algorithms, including XGBoost, have gained popularity because they can model nonlinear relationships while providing estimates of feature importance. Several comparative studies have shown that ensemble learning approaches frequently outperform conventional regression models in predicting immunotherapy outcomes [44]. Despite encouraging performance, many supervised learning studies suffer from methodological limitations, including retrospective designs, inadequate external validation, and relatively small sample sizes. Consequently, reported performance metrics may overestimate real-world clinical utility [45].

Ensemble Learning

Ensemble learning combines predictions from multiple models to improve accuracy and robustness. Random forests, gradient boosting machines, and stacked ensemble methods have demonstrated promising performance in immunotherapy prediction [46]. The principal advantage of ensemble methods lies in their ability to reduce model variance and improve generalizability. Studies in NSCLC and melanoma have reported improved prediction of durable clinical benefit and progression-free survival using ensemble approaches compared with individual algorithms [47]. Nevertheless, increased model complexity may reduce interpretability, creating challenges for clinical adoption.

Deep Learning

Deep learning represents a major methodological advancement beyond conventional radiomics. Convolutional neural networks (CNNs) can automatically learn hierarchical image representations directly from imaging data without requiring handcrafted feature extraction [48]. Several investigations have applied deep learning to CT, MRI, and PET imaging for immunotherapy response prediction. Deep learning models have demonstrated encouraging predictive performance in NSCLC, melanoma, and hepatocellular carcinoma cohorts [49]. Compared with traditional radiomics pipelines, CNNs may capture more complex spatial relationships and subtle imaging phenotypes associated with immune activity. However, deep learning approaches typically require substantially larger datasets and greater computational resources. Furthermore, their "black-box" nature raises concerns regarding interpretability and clinical trust. Consequently, integration of explainable AI techniques has become increasingly important for facilitating clinical translation [50].

Multimodal Learning and Radiogenomics

Although radiomics provides valuable information regarding tumor phenotype, immunotherapy response is influenced by a wide range of biological factors. Multimodal learning seeks to improve predictive accuracy by integrating imaging biomarkers with clinical, pathological, genomic, and molecular data [51]. Radiogenomics represents a particularly promising area of investigation. Numerous studies have reported associations between radiomic features and immune-related molecular characteristics, including PD-L1 expression, TMB, MSI status, and gene expression signatures [52]. By combining radiomic and genomic information, radiogenomic models may provide more comprehensive characterization of tumor biology and improve prediction of treatment outcomes. Recent multimodal frameworks incorporating radiomics, genomics, pathology, and clinical variables have consistently demonstrated superior performance compared with unimodal approaches [53]. Nevertheless, challenges related to data harmonization, missing information, and model complexity remain substantial barriers to implementation. Overall, current evidence suggests that machine learning significantly enhances the predictive potential of radiomics. Future progress will likely depend on development of robust, externally validated multimodal models capable of generalizing across diverse patient populations and healthcare settings.

6. Clinical Translation and Precision Oncology Applications

The ultimate goal of radiomics and machine learning research is clinical implementation. Predictive imaging biomarkers have the potential to support personalized treatment strategies by identifying patients most likely to benefit from immunotherapy while minimizing unnecessary exposure to ineffective treatments [54]. One of the most immediate applications involves patient stratification. Accurate prediction of immunotherapy response could facilitate selection of appropriate therapeutic regimens, particularly in cancers where multiple treatment options are available. Patients predicted to respond favorably may receive immunotherapy-based approaches, whereas predicted non-responders could be directed toward alternative treatments or clinical trials.

Radiomics-based models may also contribute to treatment monitoring. Quantitative imaging biomarkers can detect subtle biological changes before conventional size-based response criteria become apparent, enabling earlier assessment of therapeutic effectiveness. Such capabilities may support adaptive treatment strategies and improve clinical outcomes. Survival prediction represents another important application. Machine learning models integrating radiomic and clinical data have demonstrated encouraging performance for predicting progression-free survival and overall survival across multiple tumor types [55]. These prognostic tools may assist clinicians in risk stratification, treatment planning, and patient counseling. More broadly, radiomics and machine learning support the vision of precision oncology by transforming routinely acquired medical images into personalized biomarkers. Integration of imaging with molecular and clinical information may facilitate development of comprehensive clinical decision-support systems capable of guiding individualized cancer care.

CHALLENGES AND LIMITATIONS

Despite substantial progress, significant obstacles continue to limit widespread clinical adoption of radiomics-based immunotherapy prediction models. One of the most important challenges is the relatively small size of available datasets. Many studies include fewer than several hundred patients, increasing the risk of overfitting and limiting generalizability. This issue is particularly problematic for deep learning models, which typically require large-scale datasets to achieve robust performance. Data heterogeneity represents another major concern. Variability in imaging protocols, scanner manufacturers, reconstruction parameters, and segmentation methodologies can substantially influence radiomic feature values. Consequently, models developed at one institution often exhibit reduced performance when applied to external datasets. Segmentation variability remains a persistent source of uncertainty. Manual contouring is time-consuming and subject to interobserver variability, whereas automated segmentation methods may introduce additional errors. Because radiomic features are highly dependent on segmentation accuracy, variability at this stage can affect downstream model performance. Reproducibility is also a significant challenge. Differences in feature extraction software, preprocessing techniques, and statistical methodologies may lead to inconsistent results across studies. Although initiatives such as the Image Biomarker Standardisation Initiative have improved methodological consistency, further standardization remains necessary. Interpretability represents another important limitation. Many machine learning and deep learning models function as complex black boxes, making it difficult to understand the biological basis of their predictions. Lack of transparency may reduce clinician confidence and complicate regulatory approval processes. Regulatory and ethical considerations further complicate implementation. Clinical deployment requires rigorous validation, demonstration of safety and effectiveness, protection of patient privacy, and mitigation of algorithmic bias. Addressing these challenges will be essential for translating promising research findings into routine clinical practice.

FUTURE PERSPECTIVES

The future of radiomics and machine learning in immuno-oncology will likely be shaped by advances in artificial intelligence, data integration, and large-scale collaborative research. Foundation models trained on massive medical imaging datasets are expected to improve generalizability and reduce dependence on task-specific training data. Similarly, self-supervised learning approaches may address current limitations related to annotated dataset availability by enabling models to learn useful representations from unlabeled images. Federated learning offers another promising strategy. By allowing institutions to collaboratively train models without sharing patient-level data, federated learning may facilitate development of larger and more diverse datasets while preserving privacy. Radiogenomics and multi-omics integration are expected to become increasingly important. Combining imaging biomarkers with genomic, transcriptomic, proteomic, and immune profiling data may provide more comprehensive characterization of tumor biology and improve predictive accuracy. Large multimodal models capable of simultaneously processing imaging, clinical, pathological, and molecular information represent another emerging frontier.

These systems may ultimately support real-time clinical decision-making and personalized treatment recommendations. Finally, prospective multicenter clinical trials will be critical for validating predictive models and establishing their clinical utility. Successful integration of explainable AI, standardized methodologies, and rigorous validation frameworks will be necessary for achieving widespread adoption.

CONCLUSION

Radiomics and machine learning have emerged as powerful tools for predicting immunotherapy response in solid tumors. By extracting quantitative information from routinely acquired medical images, radiomics provides non-invasive assessment of tumor phenotype, heterogeneity, and immune-related characteristics that are difficult to capture using conventional biomarkers alone. Machine learning algorithms further enhance the predictive value of these imaging features by identifying complex patterns associated with therapeutic outcomes. Current evidence demonstrates promising applications across multiple malignancies, including NSCLC, melanoma, renal cell carcinoma, hepatocellular carcinoma, head and neck cancer, urothelial carcinoma, and colorectal cancer. Radiomics-based models have shown potential for predicting treatment response, durable clinical benefit, survival outcomes, hyperprogression, and pseudoprogression. Nevertheless, important challenges remain, including small datasets, methodological heterogeneity, reproducibility concerns, limited external validation, and regulatory barriers. Future advances in foundation models, federated learning, radiogenomics, multi-omics integration, and explainable AI may help overcome these limitations. With continued technological innovation and rigorous clinical validation, radiomics and machine learning are poised to become integral components of precision immuno-oncology, enabling more accurate patient selection, individualized treatment strategies, and improved clinical outcomes.

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