

Quantitative Radiomics of Tumour Texture Changes During Immunotherapy

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DESCRIPTION

The advent of immunotherapy has revolutionized cancer treatment, offering durable responses in malignancies previously considered refractory. Quantitative radiomics, which extracts high-dimensional imaging features to describe tumor heterogeneity, texture, and spatial complexity, has emerged as a powerful tool to assess tumor dynamics during immunotherapy and predict treatment outcomes.

Radiomics transforms standard medical images into quantitative data, capturing features that are imperceptible to the human eye. Among these, texture analysis quantifies intra-tumoral heterogeneity, including variations in intensity, shape, and spatial distribution of pixels. In the context of immunotherapy, tumor texture changes may reflect immune cell infiltration, necrosis, edema, fibrosis, and vascular remodeling—processes not always accompanied by changes in tumor size. By longitudinally evaluating these radiomic features, clinicians can gain insights into therapy-induced tumor remodeling, distinguish responders from non-responders, and anticipate immune-related adverse events.

One of the primary advantages of quantitative radiomics is its ability to capture tumor heterogeneity, a key determinant of immunotherapy response. Tumors with high heterogeneity often harbor subclones with varying immunogenicity, influencing susceptibility to Immune Checkpoint Inhibitors (ICIs). Texture features such as entropy, uniformity, and gray-level co-occurrence matrices provide metrics of heterogeneity, which can be correlated with molecular biomarkers, immune cell density, and PD-L1 expression. Studies have shown that an increase in intratumoral homogeneity after the initiation of immunotherapy often correlates with favorable responses, reflecting immune-mediated tumor remodeling and reduced subclonal variability. Conversely, persistent or increasing heterogeneity may indicate immune evasion and therapeutic resistance.

Beyond predicting response, radiomic analysis can identify early changes in tumor texture that precede volumetric changes. Conventional imaging criteria often classify tumors as stable or progressive based on size, potentially delaying clinical decision-

making. Quantitative radiomics can detect subtle textural alterations within weeks of therapy initiation, enabling early identification of responders and non-responders. For example, features capturing increased kurtosis or reduced entropy may reflect immune infiltration and necrotic regions, while changes in skewness may indicate vascular remodeling and hypoxia. Integrating these features into predictive models allows for real-time monitoring of immunotherapy efficacy and personalization of treatment schedules.

Radiomic features are often combined with clinical and molecular data in multiparametric models to improve predictive accuracy. Integration with genomic markers, Tumor Mutational Burden (TMB), Microsatellite Instability (MSI), and peripheral immune signatures provides a comprehensive view of tumor-immune interactions. Machine learning algorithms such as random forests, support vector machines, and deep learning approaches can identify the most informative radiomic signatures associated with treatment response or adverse events. These predictive models have demonstrated the potential to stratify patients, guide therapeutic escalation or de-escalation, and support clinical trial design by selecting likely responders.

Several studies have demonstrated the utility of radiomics in capturing immunotherapy-induced tumor texture changes. In metastatic melanoma, CT-based radiomic features including entropy, gray-level non-uniformity, and zone-size variance were associated with progression-free survival and overall survival following anti-PD-1 therapy. In non-small cell lung cancer, early alterations in texture features predicted response to combined chemotherapy and immunotherapy, correlating with biopsy-proven immune cell infiltration.

Despite its promise, quantitative radiomics faces several challenges that must be addressed for routine clinical translation. Standardization of imaging acquisition parameters, reconstruction algorithms, and segmentation protocols is critical to ensure reproducibility across institutions and scanners. Tumor segmentation, whether manual, semi-automated, or fully automated, significantly influences extracted features, and inter-observer variability must be minimized. Additionally, harmonization of feature extraction pipelines, feature selection, and model validation is required to prevent overfitting and

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ensure generalizability of radiomic signatures. Large, multi-institutional cohorts with prospective validation are essential to establish clinical utility.

An emerging frontier in radiomics is the integration of spatial and temporal information to capture tumor evolution during immunotherapy. Longitudinal imaging allows tracking of regional changes in texture, which may reflect immune cell trafficking, localized necrosis, or stromal remodeling. Combining radiomics with spatial transcriptomics or multiplex immunohistochemistry enables correlation of imaging features with underlying cellular and molecular processes, enhancing mechanistic understanding. Moreover, deep learning-based approaches can automatically identify complex spatiotemporal patterns, offering higher-order representations of tumor texture changes that may escape conventional analysis.

CONCLUSION

Quantitative radiomics provides a non-invasive, high-resolution approach to evaluate tumor texture changes during

immunotherapy, offering insights into intra-tumoral heterogeneity, immune infiltration, and treatment response. Longitudinal radiomic assessment can complement conventional imaging and molecular biomarkers, enabling early identification of responders, monitoring of tumor evolution, and prediction of immune-related adverse events. While challenges remain in standardization, reproducibility, and clinical validation, the integration of radiomics into clinical workflows holds promise for precision immuno-oncology. Future studies leveraging multi-modal imaging, machine learning, and spatial-molecular integration are likely to further refine radiomic models, ultimately guiding personalized immunotherapy and improving patient outcomes.