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Towards the Co-clinical Glioblastoma Treatment Paradigm - Radiomic Machine Learning Identifies Glioblastoma Gene Expression in Patients and Corresponding Xenograft Tumor Models

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Introduction

Radiomics is extraction of multi-dimensional imaging-features which when correlated with genomics is termed radiogenomics. The radio-genomic relationship has never been biologically validated. Towards creating a co-clinical glioblastoma treatment paradigm, we sought to establish causality between differential gene expression status and MRI-extracted radiomic-texture features in glioblastoma.

Methods

Radiogenomic predictions and validation were done using orthotopic xenograft models (N=40) and the Cancer Genome Atlas glioblastoma patient cohort with matched imaging (N=94). Tumor phenotypes were segmented and radiomic-features extracted using machine learning algorithms. Patients and animals were dichotomized based on Periostin (POSTN) expression levels. RNA and protein levels confirmed RNAi-mediated POSTN knockdown. Total RNAs of tumor cells isolated from mouse brains (knockdown and control) was used for microarray-based expression profiling. Radiomic-features were then utilized to predict POSTN expression status in patient and mouse, and inter-species.

Results

Our robust machine learning based analytical pipeline consists of segmentation, radiomic texture extraction, feature normalization and selection, and predictive-model generation. POSTN expression status was not associated with qualitative or volumetric MRI parameters. However, radiomic-features significantly predicted POSTN expression status in both patients (AUC 100%, sensitivity/specificity: 100%/100%) and animal model (AUC 95.24%, sensitivity/specificity: 100%/88.88%). Furthermore, texture-features in xenografts were significantly associated with humans with similar POSTN expression levels (AUC 74.36%, sensitivity/specificity: 74.42%/87.17%; p-value 0.0279).

Conclusions

We established a high degree of causality between radiomic texture-features and POSTN expression levels in a pre-clinical model with clinical validation. Our biologically validated machine learning based radiomic pipeline also showed potential application in human-mouse matched co-clinical trials and opens an avenue for the personalized co-clinical glioblastoma treatment paradigm.

Learning Objectives

MRI based machine learning unlocks untapped information from routine brain tumor imaging and allows for establishing co-clinical trial models and ultimately glioblastoma treatment paradigms to augment personalized medicine in cancer care.

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