Functional Validation of Radiogenomics with a Pre-clinical Orthotopic Glioblastoma Model

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Introduction

Intratumoral heterogeneity in Glioblastoma (GBM) is a leading causes for its dismal clinical outcome and gross total resection of GBM remains a challenge due to its aggressive invasion patterns. A clinically relevant definition of GBM heterogeneity and underlying genomic variability is urgently needed. To evaluate the true potential of radiogenomic predictions, we tested their scope in a pre-clinical setting, where glioblastoma stem cells (GSCs) were altered to express decreased levels of Periostin (POSTN), previously identified as a key pro-invasive gene. Thus generated orthotopic tumors were scanned and analyzed to identify gene specific MRI texture feature signatures, also reliably predicting the gene status in GBM patient MRI scans.

Methods

Doxycycline regulated inducible short hairpin RNA mediated knockdown of POSTN in GSC lines were established. 5X10^6 cells were implanted in nude mice frontal cortex with the help of stereotactic devices. Tumor growth was monitored by multpile MRI sequences. Region of interest (ROI) methods were applied to the rigid registration images based on axial T1-weighted imaging (T1WI) and its corresponding fluid-attenuated inversion recovery (FLAIR) sequences. Three types of textures, namely fine, medium and coarse were provided by using a Laplacian of Gaussian (LoG) filter. Rigorous statistical models such as Bootstrapping, Student T test, Linear Discriminant Analysis (LDA), Quadratic Discriminant Analysis (QDA), Naive Bayes, Multinomial dirichlet, and Gaussian Mixture Model (GMM) were applied for feature selection.

Results

We identified (specificity >95%) texture features which are highly and exclusively correlated to POSTN gene status in orthotopic mouse models. Additionally, these features were able to identify POSTN expression status in GBM patients.

Conclusions

Our results provide validation for radiogenomics, where a specific gene status can result in alterations of MRI texture features which in turn can predict gene status in an individual GBM patient.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the upcoming importance of MRI scans in tumor genetics, 2) Discuss, in small groups, the value added by this novel approach, 3) Identify further clinical applications of radilogic data in central nervous tumor research and patient care