Radiogenomic Analysis of Diffusion-Weighted MRI and Genomic Data to Inform Treatment of Glioblastoma

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Objectives: To obtain non-invasive biomarkers closely associated with the genetic subtype and gene signatures through an integrative analysis of imaging and gene expression data of Glioblastoma (GBM) patients.

Methods: In this retrospective study, we analyzed the expression of 12,042 genes for 558 patients from The Cancer Genome Atlas and diffusion weighted (DW) MRI for 50 of these 558 patients from the Cancer Imaging Archive. We identified the contrast enhancing region of the tumors using contrast-enhanced T1-weighted MRI images and computed the mean apparent diffusion coefficient (mADC) from DW-MRI images. Using the gene expression data, we classified patients into GBM subtypes\(^1\), determined the number and composition of genes modules using the gap statistic, and computed gene signature scores. We used logistic regression to assess mADC as a subtype predictor and compare mADC among subtypes using Mann-Whitney-U tests. We computed Spearman correlations to determine the associations between mADC and each gene signature. We performed gene enrichment analysis using Ingenuity Pathway Analysis. We adjusted p-values using Benjamini-Hochberg method.

Results: The mADC was a significant predictor for the neural subtype. Neural tumors had a significantly lower mADC compared to non-neural tumors (p<0.01), with mADC of \(1.07\pm0.16\times10^{-3}\) mm\(^2\)/s and \(1.23\pm0.16\times10^{-3}\) mm\(^2\)/s for neural and non-neural tumors, respectively. We found eight gene modules in the GBM cohort. The mADC was statistically significantly correlated with the gene signature related with dendritic cell maturation (\(\rho=-0.51, p<0.01\)).

Conclusions: The mADC was able to identify the set of patients with neural tumors non-invasively. Patients with neural tumors do not benefit from a more aggressive standard-of-care therapy\(^1\), so the mADC could help inform treatment. The mADC can also be used as a biomarker of a gene signature that is related with dendritic cell maturation. This result suggests that mADC could potentially be used to help identify the patients with immunogenic tumors and therefore, assist in clinical trial design for immunotherapies.
